OFFICE HE HE TED STATES PATENT AND TRADEM! IN THE, FOR FILING APPLICATION UNDER F 53(b) Atty Dkt.: 2752-15 Bant to 37 CFR 1.53(b), please file a X continuation/ divisional C# M# Spending prior PATENT APPLICATION of: Date: August 15, 2000 MAERTENS et al. Group: 1633 No. 08/362,455 Examiner: Martinell, J Fanuary 11, 1995
FOR NEW SEQUENCES OF HEPATITIS C VIRUS GENOTYPES AND THEIR USE AS THERAPEUTIC AND DIAGNOSTIC AGENTS Assistant Commissioner for Patents Washington, DC 20231 Sir: This request for filing under Rule 53(b) is made by the following named inventor(s) (using the above-identified title): Inventor(s): MAERTENS et al. Attached is a true copy of the prior application as originally filed including the specification, claims, Sequence Listing, Oath/Declaration and drawings (if any) and abstract (if any). No amendments (if any) referenced in the Oath or ١, Declaration filed to complete the prior application introduced new matter. Priority is hereby claimed under 35 USC 119 based on the following foreign applications, the entire content of which is hereby incorporated by reference in this application: Day/Month/Year/Filed Country **Application Number** 27/April/1993 Europe 93.401 099.2 05/August/1993 Europe 93.402.019.9 27/April/1994 International PCT/EP94/01323 certified copy(ies) of foreign application(s) attached or Đ already filed on in prior appln. no. M April 27, 1994 already filed in PCT/EP94/01323 The prior application is assigned to N.V. INNOGENETICS S.A.. Power of Attorney has been granted to Thomas E. Byrne et al, Reg. No. 32,205 of Nixon & Vanderhye P.C., 1100 N. Glebe Rd., 8th Flr, Arlington, VA 22201. Address all future communications to: Nixon & Vanderhye P.C., 1100 N. Glebe Rd., 8th Floor, Arlington, VA 22201. Please amend the specification by inserting before the first line -- This is a continuation of application Serial No. 08/362,455, filed January 11, 1995, allowed, which is a 371 application of PCT/EP94/01323, filed April 27, 1994, the entire content of which is hereby incorporated by reference in this application .--Petition filed in prior application to extend its life to insure copendency. The Examiner's attention is directed to the prior art cited in the parent application by applicant and/or Examiner for the reasons stated therein and return of an initialed copy of the attached PTO-1449 Form listing same, pursuant to MPEP \$609, are requested. Please enter the attached and/or below preliminary amendment prior to calculation of filing fee: **ATTACHED** The entire disclosure of the prior application above-referenced is considered as being part of the disclosure of this new application and is hereby incorporated by reference therein. FILING FEE IS BASED ON CLAIMS AS FILED LESS ANY HEREWITH CANCELED 690.00 Basic Filing Fee \$ 54.00 x \$ 18.00 3 Total effective claims - 20 (at least 20) = \$ 0.00 0 x \$ 78.00 - 3 (at least 3) = Independent claims 1 0.00 If any proper multiple dependent claims now added for first time, add \$260.00 (ignore improper) **SUBTOTAL** 744.00 0.00)If "small entity," then enter half (1/2) of subtotal and subtract 744.00 SECOND SUBTOTAL 0.00 Assignment Recording Fee (\$40.00) 744.00 **TOTAL FEE ENCLOSED \$** Any future submission requiring an extension of time is hereby stated to include a petition for such time extension.

Any future submission requiring an extension of time is hereby stated to include a petition for such time extension. The Commissioner is hereby authorized to charge any <u>deficiency</u> in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our **Account No. 14-1140.** A <u>duplicate</u> copy of this sheet is attached.

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NEW SEQUENCES OF HEPATITIS C VIRUS GENOTYPES AND THEIR USE AS THERAPEUTIC AND DIAGNOSTIC AGENTS

The invention relates to new sequences of hepatitis C virus (HCV) genotypes and their use as therapeutic and diagnostic agents.

The present invention relates to new nucleotide and amino acid sequences corresponding to the coding region of a new type 2 subtype 2d, type-specific sequences corresponding to HCV type 3a, to new sequences corresponding to the coding region of a new subtype 3c, and to new sequences corresponding to the coding region of HCV type 4 and type 5 subtype 5a: a process for preparing them, and their use for diagnosis, prophylaxis and therapy.

The technical problem underlying the present invention is to provide new type-specific sequences of the Core, the E1, the E2, the NS3, the NS4 and the NS5 regions of HCV type 4 and type 5, as well as of new variants of HCV types 2 and 3. These new HCV sequences are useful to diagnose the presence of type 2 and/or type 3 and/or type 4 and/or type 5 HCV genotypes in a biological sample. Moreover, the availability of these new type-specific sequences can increase the overall sensitivity of HCV detection and should also prove to be useful for therapeutic purposes.

Hepatitis C viruses (HCV) have been found to be the major cause of non-A, non-B hepatitis. The sequences of cDNA clones covering the complete genome of several prototype isolates have been determined (Kato et al., 1990; Choo et al., 1991; Okamoto et al., 1991; Okamoto et al., 1992). Comparison of these isolates shows that the variability in nucleotide sequences can be used to distinguish at least 2 different genotypes, type 1 (HCV-1 and HCV-J) and type 2 (HC-J6 and HC-J8), with an average homology of about 68%. Within each type, at least two subtypes exist (e.g. represented by HCV-1 and HCV-J), having an average homology of about 79%. HCV genomes belonging to the same subtype show average homologies of more than 90% (Okamoto et al., 1992). However, the partial nucleotide sequence of the NS5 region of the HCV-T isolates showed at most 67% homology with the previously published sequences, indicating the existence of a yet another HCV type (Mori et al., 1992). Parts of the 5' untranslated region (UR), core, NS3, and NS5 regions of this type 3 have been published, further establishing the similar evolutionary distances between the 3 major genotypes and their subtypes (Chan et al., 1992).

The identification of type 3 genotypes in clinical samples can be achieved by means of PCR with type-specific primers for the NS5 region. However, the degree to which this will

be successful is largely dependent on sequence variability and on the virus titer present in the serum. Therefore, routine PCR in the open reading frame, especially for type 3 and the new type 4 and 5 described in the present invention and/or group V (Cha et al., 1992) genotypes can be predicted to be unsuccessful. A new typing system (LiPA), based on variation in the highly conserved 5' UR, proved to be more useful because the 5 major HCV genotypes and their subtypes can be determined (Stuyver et al., 1993). The selection of high-titer isolates enables to obtain PCR fragments for cloning with only 2 primers, while nested PCR requires that 4 primers match the unknown sequences of the new type 3, 4 and 5 genotypes.

New sequences of the 5' untranslated region (5'UR) have been listed by Bukh et al. (1992). For some of these, the E1 region has recently been described (Bukh et al., 1993). Isolates with similar sequences in the 5'UR to a group of isolates including DK12 and HK10 described by Bukh et al. (1992) and E-b1 to E-b8 described and classified as type 3 by Chan et al. (1991), have been reported and described in the 5'UR, the carboxyterminal part of E1, and in the NS5 region as group IV by Cha et al. (1992; WO 92/19743), and have also been described in the 5'UR for isolate BR56 and classified as type 3 by the inventors of this application (Stuyver et al., 1993).

The aim of the present invention is to provide new HCV nucleotide and amino acid sequences enabling the detection of HCV infection.

Another aim of the present infection is to provide new nucleotide and amino acid HCV sequences enabling the classification of infected biological fluids into different serological groups unambiguously linked to types and subtypes at the genome level.

Another aim of the present invention is to provide new nucleotide and amino acid HCV sequences ameliorating the overall HCV detection rate.

Another aim of the present invention is to provide new HCV sequences, useful for the design of HCV vaccine compositions.

Another aim of the present invention is to provide a pharmaceutical composition consisting of antibodies raised against the polypeptides encoded by these new HCV sequences, for therapy or diagnosis.

The present invention relates more particularly to a composition comprising or consisting of at least one polynucleic acid containing at least 5, and preferably 8 or more contiguous nucleotides selected from at least one of the following HCV sequences:

- an HCV type 3 genomic sequence, more particularly in any of the following regions:

- the region spanning positions 417 to 957 of the Core/E1 region of HCV subtype 3a,
- the region spanning positions 4664 to 4730 of the NS3 region of HCV type 3,
- the region spanning positions 4892 to 5292 of the NS3/4 region of HCV type 3,
- the region spanning positions 8023 to 8235 of the NS5 region of the BR36 subgroup of HCV subtype 3a,
- an HCV subtype 3c genomic sequence,

more particularly the coding regions of the above-specified regions;

- an HCV subtype 2d genomic sequence, more particularly the coding region of HCV subtype 2d;
- an HCV type 4 genomic sequence, more particularly the coding region, more particularly the coding region of subtypes 4a, 4e, 4f, 4g, 4h, 4i, and 4j.
- an HCV type 5 genomic sequence, more particularly the coding region of HCV type 5, more particularly the regions encoding Core, E1, E2, NS3, and NS4

with said nucleotide numbering being with respect to the numbering of HCV nucleic acids as shown in Table 1, and with said polynucleic acids containing at least one nucleotide difference with known HCV (type 1, type 2, and type 3) polynucleic acid sequences in the above-indicated regions, or the complement thereof.

It is to be noted that the nucleotide difference in the polynucleic acids of the invention may involve or not an amino acid difference in the corresponding amino acid sequences coded by said polynucleic acids.

According to a preferred embodiment, the present invention relates to a composition comprising or containing at least one polynucleic acid encoding an HCV polyprotein, with said polynucleic acid containing at least 5, preferably at least 8 nucleotides corresponding to at least part of an HCV nucleotide sequence encoding an HCV polyprotein, and with said HCV polyprotein containing in its sequence at least one of the following amino acid residues: L7, Q43, M44, S60, R67, Q70, T71, A79, A87, N106, K115, A127, A190, S130, V134, G142, I144, E152, A157, V158, P165, S177 or Y177, I178, V180 or E180 or F182, R184, I186, H187, T189, A190, S191 or G191, Q192 or L192 or I192 or V192 or E192, N193 or H193 or P193, W194 or Y194, H195, A197 or I197 or V197 or T197, V202, I203 or L203, Q208, A210, V212, F214, T216, R217 or D217 or E217 or V217, H218 or N218, H219 or

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V219 or L219, L227 or I227, M231 or E231 or Q231, T232 or D232 or A232 or K232, Q235 or I235, A237 or T237, I242, I246, S247, S248, V249, S250 or Y250, I251 or V251 or M251 or F251, D252, T254 or V254, L255 or V255, E256 or A256, M258 or F258 or V258, A260 or Q260 or S260, A261, T264 or Y264, M255, I266 or A266, A267, G268 or T268, F271 or M271 or V271, I277, M280 or H280, I284 or A284 or L84, V274, V291 N292 or S292, R293 or I293 or Y293, Q294 or R294, L297 or I297 or Q297, A299 or K299 or Q299, N303 or T303, T308 or L308, T310 or F310 or A310 or D310 or V310, L313. G317 or Q317, L333, S351, A358, A359, A363, S364, A366, T369, L373, F376, Q386, I387, S392, I399, F402, I403, R405, D454, A461, A463, T464, K484, Q500, E501, S521. K522, H524, N528, S531, S532, V534, F536, F537, M539, I546, C1282, A1283, H1310, V1312, Q1321, P1368, V1372, V1373, K1405, Q1406, S1409, A1424, A1429, C1435, \$1436, \$1456, H1496, A1504, D1510, D1529, I1543, N1567, D1556, N1567, M1572. Q1579, L1581, S1583, F1585, V1595, E1606 or T1606, M1611, V1612 or L1612, P1630. C1636, P1651, T1656 or I1656, L1663, V1667, V1677, A1681, H1685, E1687, G1689. V1695, A1700, Q1704, Y1705, A1713, A1714 or S1714, M1718, D1719, A1721 or T1721, R1722, A1723 or V1723, H1726 or G1726, E1730, V1732, F1735, I1736, S1737, R1738, T1739, G1740, Q1741, K1742, Q1743, A1744, T1745, L1746, E1747 or K1747, I1749. A1750, T1751 or A1751, V1753, N1755, K1756, A1757, P1758, A1759, H1762, T1763, Y1764, P2645, A2647, K2650, K2653 or L2653, S2664, N2673, F2680, K2681, L2686. H2692, Q2695 or L2695 or I2695, V2712, F2715, V2719 or Q2719, T2722, T2724, S2725. R2726, G2729, Y2735, H2739, I2748, G2746 or I2746, I2748, P2752 or K2752, P2754 or T2754, T2757 or P2757, with said notation being composed of a letter representing the amino acid residue by its one-letter code, and a number representing the amino acid numbering according to Kato et al., 1990.

Each of the above-mentioned residues can be found in any of Figures 2, 5, 7, 11 or 12 showing the new amino acid sequences of the present invention aligned with known sequences of other types or subtypes of HCV for the Core, E1, E2, NS3, NS4, and NS5 regions.

More particularly, a polynucleic acid contained in the composition according to the present invention contains at least 5, preferably 8, or more contiguous nucleotides corresponding to a sequence of contiguous nucleotides selected from at least one of HCV sequences encoding the following new HCV amino acid sequences:

- new sequences spanning amino acid positions 1 to 319 of the Core/E1 region of HCV subtype 2d, type 3 (more particularly new sequences for subtypes 3a and 3c), new type 4

subtypes (more particularly new sequences for subtypes 4a, 4e, 4f, 4g, 4h, 4i and 4j) and type 5a, as shown in Figure 5;

- new sequences spanning amino acid positions 328 to 546 of the E1/E2 region of HCV subtype 5a as shown in Figure 12;
- new sequences spanning amino acid positions 1556 to 1764 of the NS3/NS4 region of HCV type 3 (more particularly for new subtypes 3a sequences), and subtype 5a, as shown in Figure 7 or 11;
- new sequences spanning amino acid positions 2645 to 2757 of the NS5B region of HCV subtype 2d, type 3 (more particularly for new subtypes 3a and 3c), new type 4 subtypes (more particularly subtypes 4a, 4e, 4f, 4g, 4h, 4i and 4j) and subtype 5a, as shown in Figure 2,

Using the LiPA system mentioned above, Brazilian blood donors with high titer type 3 hepatitis C virus, Gabonese patients with high-titer type 4 hepatitis C virus, and a Belgian patient with high-titer HCV type 5 infection were selected. Nucleotide sequences in the core, E1, NS5 and NS4 regions which have not yet been reported before, were analyzed in the frame of the invention. Coding sequences (with the exception of the core region) of any type 4 isolate are reported for the first time in the present invention. The NS5b region was also analyzed for the new type 3 isolates. After having determined the NS5b sequences, comparison with the Ta and Tb subtypes described by Mori et al. (1992) was possible, and the type 3 sequences could be identified as type 3a genotypes. The new type 4 isolates segregated into 10 subtypes, based on homologies obtained in the NS5 and E1 regions. New type 2 and 3 sequences could also be distinguished from previously described type 2 or 3 subtypes from sera collected in Belgium and the Netherlands.

The term "polynucleic acid" refers to a single stranded or double stranded nucleic acid sequence which may contain at least 5 contiguous nucleotides to the complete nucleotide sequence (f.i. at least 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or more contiguous nucleotides). A polynucleic acid which is up till about 100 nucleotides in length is often also referred to as an oligonucleotide. A polynucleic acid may consist of deoxyribonucleotides or ribonucleotides, nucleotide analogues or modified nucleotides, or may have been adapted for therapeutic purposes. A polynucleic acid may also comprise a double stranded cDNA clone which can be used for cloning purposes, or for *in vivo* therapy, or prophylaxis.

The term "polynucleic acid composition" refers to any kind of composition comprising essentially said polynucleic acids. Said composition may be of a diagnostic or a therapeutic

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nature.

The expression "nucleotides corresponding to" refers to nucleotides which are homologous or complementary to an indicated nucleotide sequence or region within a specific HCV sequence.

The term "coding region" corresponds to the region of the HCV genome that encodes the HCV polyprotein. In fact, it comprises the complete genome with the exception of the 5' untranslated region and 3' untranslated region.

The term "HCV polyprotein" refers to the HCV polyprotein of the HCV-J isolate (Kato et al., 1990). The adenine residue at position 330 (Kato et al., 1990) is the first residue of the ATG codon that initiates the long HCV polyprotein of 3010 amino acids in HCV-J and other type 1b isolates, and of 3011 amino acids in HCV-1 and other type 1a isolates, and of 3033 amino acids in type 2 isolates HC-J6 and HC-J8 (Okamoto et al., 1992).

This adenine is designated as position 1 at the nucleic acid level, and this methionine is designated as position 1 at the amino acid level, in the present invention. As type 1a isolates contain 1 extra amino acid in the NS5a region, coding sequences of type 1a and 1b have identical numbering in the Core, E1, NS3, and NS4 region, but will differ in the NS5b region as indicated in Table 1. Type 2 isolates have 4 extra amino acids in the E2 region, and 17 or 18 extra amino acids in

the NS5 region compared to type 1 isolates, and will differ in numbering from type 1 isolates in the NS3/4 region and NS5b regions as indicated in Table 1.

TABLE 1

	Region	Positions described in the present invention*	Positions described for HCV-J (Kato et al., 1990)	Positions described for HCV-1 (Choo et al., 1991)	Positions described for HC-J6. HC-J8 (Okamoto et al., 1992)
Nucleotide s	NS5b	8023/8235 7932/8271	8352/8564 8261/8600	8026/8238 7935/8274	8433/8645 8342/8681
	NS3/4	4664/5292 4664/4730 4892/5292 3856/4209 4936/5292	4993/5621 4993/5059 5221/5621 4185/4528 5265/5621	4664/5292 4664/4730 4892/5292 3856/4209 4936/5292	5017.5645 5017/5083 5245/5645 4209 4762 5289 5645
		coding region of present invention	330.9359	1/9033	342/9439
Amino Acids	NS5b	2675/2745 2645/2757	2675/2745 2645/2757	2676/2746 2646/2758	2698/2768 2668/2780
	NS3/4	1556/1764 1286/1403 1646/1764	1556/1764 1286/1403 1646/1764	1556/1764 1286/1403 1646/1764	1560/1768 1290/1407 1650/1768

Table 1 Comparison of the HCV nucleotide and amino acid numbering system used in the present invention (*) with the numbering used for other prototype isolates. For example, 8352/8564 indicates the region designated by the numbering from nucleotide 8352 to nucleotide 8564 as described by Kato et al. (1990). Since the numbering system of the present invention starts at the polyprotein initiation site, the 329 nucleotides of the 5° untranslated region described by Kato et al. (1990) have to be substracted, and the corresponding region is numbered from nucleotide 8023 ("8352-329") to 8235 ("8564-329")

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The term "HCV type" corresponds to a group of HCV isolates of which the complete genome shows more than 74% homology at the nucleic acid level, or of which the NS5 region between nucleotide positions 7932 and 8271 shows more than 74% homology at the nucleic acid level, or of which the complete HCV polyprotein shows more than 78% homology at the amino acid level, or of which the NS5 region between amino acids at positions 2645 and 275? shows more than 80% homology at the amino acid level, to polyproteins of the other isolates of the group, with said numbering beginning at the first ATG codon or first methionine of the long HCV polyprotein of the HCV-J isolate (Kato et al., 1990). Isolates belonging to different types of HCV exhibit homologies, over the complete genome, of less than 74% at the nucleic acid level and less than 78% at the amino acid level. Isolates belonging to the same type usually show homologies of about 92 to 95% at the nucleic acid level and 95 to 96% at the amino acid level when belonging to the same subtype, and those belonging to the same type but different subtypes preferably show homologies of about 79% at the nucleic acid level and 85-86% at the amino acid level.

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More preferably the definition of HCV types is concluded from the classification of HCV isolates according to their nucleotide distances calculated as detailed below.

- (1) based on phylogenetic analysis of nucleic acid sequences in the NS50 region between nucleotides 7935 and 8274 (Choo et al., 1991) or 8261 and 8600 (Kato et al., 1990) or 8342 and 8681 (Okamoto et al., 1991), isolates belonging to the same HCV type show nucleotide distances of less than 0.34, usually less than 0.33, and more usually of less than 0.32, and isolates belonging to the same subtype show nucleotide distances of less than 0.135, usually of less than 0.13, and more usually of less than 0.125, and consequently isolates belonging to the same type but different subtypes show nucleotide distances ranging from 0.135 to 0.34, usually ranging from 0.1384 to 0.2477, and more usually ranging from 0.15 to 0.32, and isolates belonging to different HCV types show nucleotide distances greater than 0.34, usually greater that 0.35, and more usually of greater than 0.358, more usually ranging from 0.1384 to 0.2977.
- (2) based on phylogenetic analysis of nucleic acid sequences in the core/E1 region between nucleotides 378 and 957, isolates belonging to the same HCV type show nucleotide distances of less than 0.38, usually of less than 0.37, and more usually of less than 0.364, and isolates belonging to the same subtype show nucleotide distances of less than 0.17, usually of less than 0.16, and more usually of less than 0.15, more usually less than 0.135, more usually less than 0.134, and consequently isolates belonging to the same type but different subtypes show

nucleotide distances ranging from 0.15 to 0.38, usually ranging from 0.16 to 0.37, and more usually ranging from 0.17 to 0.36, more usually ranging from 0.133 to 0.379, and isolates belonging to different HCV types show nucleotide distances greater than 0.34, 0.35, 0.36, usually more than 0.365, and more usually of greater than 0.37,

(3) based on phylogenetic analysis of nucleic acid sequences in the NS3/NS4 region between nucleotides 4664 and 5292 (Choo et al., 1991) or between nucleotides 4993 and 5621 (Kato et al., 1990) or between nucleotides 5017 and 5645 (Okamoto et al., 1991), isolates belonging to the same HCV type show nucleotide distances of less than 0.35, usually of less than 0.34, and more usually of less than 0.33, and isolates belonging to the same subtype show nucleotide distances of less than 0.19, usually of less than 0.18, and more usually of less than 0.17, and consequently isolates belonging to the same type but different subtypes show nucleotide distances ranging from 0.17 to 0.35, usually ranging from 0.18 to 0.34, and more usually ranging from 0.19 to 0.33, and isolates belonging to different HCV types show nucleotide distances greater than 0.33, usually greater than 0.34, and more usually of greater than 0.35.

Table 2 · Molecular evolutionary distances

Region	Core/E1	E1	NS5B	NS5B
	579 bp	384 bp	340 bp	222 bp
Isolates*	0.0017 - 0.1347	0.0026 - 0 2031	0.0003 - 0.1151	0 000 - 0.1323
	(0.0750 <u>+</u> 0.0245)	(0.0969 <u>+</u> 0 0239)	(0.0637 <u>÷</u> 0.0229)	(0 0607 <u>+</u> 0.0205)
Subtypes*	0.1330 - 0.3794	0.1645 - 0.4869	0.1384 - 0.2977	0 117 - 0.3538
	(0.2786 <u>+</u> 0.0363)	(0.3761 <u>+</u> 0.0433)	(0.2219 <u>-</u> 0.0341)	(0 2391 <u>+</u> 0 0399)
Types	0.3479 - 0.6306 (0.4703 <u>+</u> 0.0525)	0.4309 - 0.9561 (0.6308 <u>+</u> 0.0928)	0.3581 - 0.6670 (0 4994 ± 0.0495)	$0.3457 - 0.7471$ (0.5295 ± 0.0627)

Figures created by the PHYLIP program DNADIST are expressed as minimum to maximum (average ± standard deviation). Phylogenetic distances for isolates belonging to the same subtype ('isolates'), to different subtypes of the same type ('subtypes'), and to different types ('types') are given.

In a comparative phylogenetic analysis of available sequences, ranges of molecular evolutionary distances for different regions of the genome were calculated, based on 19,78!

pairwise comparisons by means of the DNA DIST program of the phylogeny inference package PHYLIP version 3.5C (Felsenstein, 1993). The results are shown in Table 2 and indicate that although the majority of distances obtained in each region fit with classification of a certain isolate, only the ranges obtained in the 340bp NS5B-region are non-overlapping and therefor conclusive. However, as was performed in the present invention, it is preferable to obtain sequence information from at least 2 regions before final classification of a given isolate.

Designation of a number to the different types of HCV and HCV types nomenclature is based on chronological discovery of the different types. The numbering system used in the present invention might still fluctuate according to international conventions or guidelines. For example, "type 4" might be changed into "type 5" or "type 6".

The term "subtype" corresponds to a group of HCV isolates of which the complete polyprotein shows a homology of more than 90% both at the nucleic acid and amino acid levels, or of which the NS5 region between nucleotide positions 7932 and 8271 shows a homology of more than 90% at the nucleic acid level to the corresponding parts of the genomes of the other isolates of the same group, with said numbering beginning with the adenine residue of the initiation codon of the HCV polyprotein. Isolates belonging to the same type but different subtypes of HCV show homologies of more than 74% at the nucleic acid level and of more than 78% at the amino acid level.

The term "BR36 subgroup" refers to a group of type 3a HCV isolates (BR36, BR33, BR34) that are 95 %, preferably 95.5 %, most preferably 96 % homologous to the sequences as represented in SEQ ID NO 1, 3, 5, 7, 9, 11 in the NS5b region from position 8023 to 8235.

It is to be understood that extremely variable regions like the E1, E2 and NS4 regions will exhibit lower homologies than the average homology of the complete genome of the polyprotein.

Using these criteria, HCV isolates can be classified into at least 6 types. Several subtypes can clearly be distinguished in types 1, 2, 3 and 4: 1a, 1b, 2a, 2b, 2c, 2d, 3a, 3b, 4a, 4b, 4c, 4d, 4e, 4f, 4g, 4h, 4i and 4j based on homologies of the 5' UR and coding regions including the part of NS5 between positions 7932 and 8271. An overview of most of the reported isolates and their proposed classification according to the typing system of the present invention as well as other proposed classifications is presented in Table 3.

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Table 3

HCV CLASSIFICATION

-	OKA- MOTO	MORI	NAKA O	СНА	PROTOTYPE
1a	I	I	Pt	GI	HCV-1, HCV-H, HC-JI
16	II	П	KI	GII	HCV-J, HCV-BK, HCV-T, HC-JK1, HC-J4, HCV-CHINA
lc					HC-G9
2a	Ш	Ш	K2a	GШ	HC-J6
2ь	ľV	ľV	К2ъ	GΠI	HC-J8
2c					\$83, ARG6, ARG8, IIO, T983
2d					NE92
3a	v	v	K 3	GIV	E-b1, Ta, BR36, BR33, HD10, NZL1
3ъ		VI	K3	GIV	HCV-TR, T₀
3c					BE98
4a					Z4, GB809-4
4b					Z 1
4c					GB116, GB358, GB215, Z6, Z7
4 d					DK13
4e					GB809-2, CAM600, CAM736
4f					CAM622, CAM627
4g					GB549
4h					GB438
4 i					CAR4/1205
4 j					CAR1/501
4k					EG29
5a				GV	\$A3, \$A4, \$A1, \$A7, \$A11, BE95
6a					HK1, HK2, HK3, HK4

The term "complement" refers to a nucleotide sequence which is complementary to an indicated sequence and which is able to hybridize to the indicated sequences.

The composition of the invention can comprise many combinations. By way of example, the composition of the invention can comprise:

- two (or more) nucleic acids from the same region or,
- two nucleic acids (or more), respectively from different regions, for the same isolate or for different isolates.
- or nucleic acids from the same regions and from at least two different regions (for the same isolate or for different isolates).

The present invention relates more particularly to a polynucleic acid composition as defined above, wherein said polynucleic acid corresponds to a nucleotide sequence selected from any of the following HCV type 3 genomic sequences:

- an HCV genomic sequence having a homology of at least 67%, preferably more than 69%, more preferably 71%, even more preferably more than 73%, or most preferably more than 76% to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 (HD10, BR36 or BR33 sequences) in the region spanning positions 417 to 957 of the Core/E1 region as shown in Figure 4;
- an HCV genomic sequence having a homology of at least 65%, preferably more than 67%, preferably more than 69%, even preferably more than 70%, most preferably more than 74% to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 (HD10, BR36 or BR33 sequences) in the region spanning positions 574 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence as having a homology of at least 79%, more preferably at least 81%, most preferably more than 83% or more to any of the sequences as represented in SEQ ID NO 147 (representing positions 1 to 346 of the Core region of HVC type 3c, sequence BE98) in the region spanning positions 1 to 378 of the Core region as shown in Figure 3;
- an HCV genomic sequence of HVC type 3a having a homology of at least 74%, more preferably at least 76%, most preferably more than 78% or more to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 (HD10, BR36 or BR33 sequences) in the region spanning positions 417 to 957 in the Core/E1 region as shown in Figure 4;
- an HCV genomic sequence of HCV type 3a as having a homology of at least 74%,

preferably more than 76%, most preferably 78% or more to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 (HD10, BR36 or BR33 sequences) in the region spanning positions 574 to 957 in the E1 region as shown in Figure 4;

- an HCV genomic sequence as having a homology of more than 73.5%, preferably more than 74%, most preferably 75% homology to the sequence as represented in SEQ ID NO 29 (HCCl53 sequence) in the region spanning positions 4664 to 4730 of the NS3 region as shown in figure 6;
- an HCV genomic sequence having a homology of more than 70%, preferably more than 72%, most preferably more than 74% homology to any of the sequences as represented in SEQ ID NO 29, 31, 33, 35, 37 or 39 (HCCl53, HD10, BR36 sequences) in the region spanning positions 4892 to 5292 in the NS3/NS4 region as shown in Figure 6 or 10;
- an HCV genomic sequence of the BR36 subgroup of HCV type 3a as having a homology of more than 95%, preferably 95,5%, most preferably 96% homology to any of the sequences as represented in SEQ ID NO 5, 7, 1, 3, 9 or 11 (BR34, BR33, BR36 sequences) in the region spanning positions 8023 to 8235 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence of the BR36 subgroup of HCV type 3a as having a homology of more than 96%, preferably 96.5%, most preferably 97% homology to any of the sequences as represented in SEQ ID NO 5, 7, 1, 3, 9 or 11 (BR34, BR33, BR36 sequences) in the region spanning positions 8023 to 8192 of the NS5B region as shown in Figure 1;
- an HCV genomic sequence of HCV type 3c being characterized as having a homology of more than 79%, more preferably more than 81%, and most preferably more than 83% to the sequence as represented in SEQ ID NO 149 (BE98 sequence) in the region spanning positions 7932 to 8271 in the NS5B region as shown in Figure 1.

Preferentially the above-mentioned genomic HCV sequences depict sequences from the coding regions of all the above-mentioned sequences.

According to the nucleotide distance classification system (with said nucleotide distances being calculated as explained above), said sequences of said composition are selected from:

- an HCV genomic sequence being characterized as having a nucleotide distance of less than 0.44, preferably of less than 0.40, most preferably of less than 0.36 to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 in the region

spanning positions 417 to 957 of the Core/El region as shown in Figure 4;

- an HCV genomic sequence being characterized having a nucleotide distance of less than 0.53, preferably less than 0.49, most preferably of less than 0.45 to any of the sequences as represented in SEQ ID NO 19, 21, 23, 25 or 27 in the region spanning positions 574 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence characterized having a nucleotide distance of less than 0.15, preferably less than 0.13, and most preferably less than 0.11 to any of the sequences as represented in SEQ ID NO 147 in the region spanning positions 1 to 378 of the Core region as shown in Figure 3;
- an HCV genomic sequence of HVC type 3a being characterized as having a nucleotide distance of less than 0.3, preferably less than 0.26, most preferably of less than 0.22 to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 in the region spanning positions 417 to 957 in the Core/E1 region as shown in Figure 4;
- an HCV genomic sequence of HCV type 3a being characterized as having a nucleotide distance of less than 0.35, preferably less than 0.31, most preferably of less than 0.27 to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 in the region spanning positions 574 to 957 in the E1 region as shown in Figure 4;
- an HCV genomic sequence of the BR36 subgroup of HCV type 3a being characterized as having a nucleotide sequence of less than 0.0423, preferably less than 0.042, preferably less than 0.0362 to any of the sequences as represented in SEQ ID NO 5, 7, 1, 3, 9 or 11 in the region spanning positions 8023 to 8235 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence of HCV type 3c being characterized as having a nucleotide distance of less than 0.255, preferably of less than 0.25, more preferably of less than 0.21, most preferably of less than 0.17 to the sequence as represented in SEQ ID NO 149 in the region spanning positions 7932 to 8271 in the NS5B region as shown in Figure 1.

In the present application, the E1 sequences encoding the antigenic ectodomain of the E1 protein, which does not overlap the carboxyterminal signal-anchor sequences of E1 disclosed by Cha et al. (1992; WO 92/19743), in addition to the NS4 epitope region, and a part of the NS5 region are disclosed for 4 different isolates: BR33, BR34, BR36, HCCl53 and HD10, all belonging to type 3a (SEQ ID NO 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 35, 37 or 39).

Also within the present invention are new subtype 3c sequences (SEQ ID NO 147, 149 of the isolate BE98 in the Core and NS5 regions (see Figures 3 and 1).

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Finally the present invention also relates to a new subtype 3a sequence as represented in SEQ ID NO 217 (see Figure 1)

Also included within the present invention are sequence variants of the polynucleic acids as selected from any of the nucleotide sequences as given in any of the above mentioned SEQ ID numbers, with said sequence variants containing either deletions and/or insertions of one or more nucleotides, mainly at the extremities of oligonucleotides (either 3' or 5'), or substitutions of some non-essential nucleotides by others (including modified nucleotides an/or inosine), for example, a type 1 or 2 sequence might be modified into a type 3 sequence by replacing some nucleotides of the type 1 or 2 sequence with type-specific nucleotides of type 3 as shown in Figure 1 (NS5 region), Figure 3 (Core region), Figure 4 (Core/E1 region). Figure 6 and 10 (NS3/NS4 region).

According to another embodiment, the present invention relates to a polynucleic acid composition as defined above, wherein said polynucleic acids correspond to a nucleotide sequence selected from any of the following HCV type 5 genomic sequences:

- an HCV genomic sequence as having a homology of more than 85%, preferably more than 86%, most preferably more than 87% homology to any of the sequences as represented in SEQ ID NO 41, 43, 45, 47, 49, 51, 53 (PC sequences) or 151 (BE95 sequence) in the region spanning positions 1 to 573 of the Core region as shown in Figure 9 and 3;
- an HCV genomic sequence as having a homology of more than 61%, preferably more than 63%, more preferably more than 65% homology, even more preferably more than 66% homology and most preferably more than 67% homology (f.i. 69 and 71%) to any of the sequences as represented in SEQ ID NO 41, 43, 45, 47, 49, 51, 53 (PC sequences). 153 or 155 (BE95, BE100 sequences) in the region spanning positions 574 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence having a homology of more than 76.5%, preferably of more than 77%, most preferably of more than 78% homology with any of the sequences as represented in SEQ ID NO 55, 57, 197 or 199 (PC sequences) in the region spanning positions 3856 to 4209 of the NS3 region as shown in Figure 6 or 10;
- an HCV genomic sequence having a homology of more than 68%, preferably of more than 70%, most preferably of more than 72% homology with the sequence as represented in SEQ ID NO 157 (BE95 sequence) in the region spanning positions 980 to 1179 of the E1/E2 region as shown in Figure 13;
- an HCV genomic sequence having a homology of more than 57%, preferably more than

59%, most preferably more than 61% homology to any of the sequences as represented in SEQ ID NO 59 or 61 (PC sequences) in the region spanning positions 4936 to 5296 of the NS4 region as shown in Figure 6 or 10;

- an HCV genomic sequence as having a homology of more than 93%, preferably more than 93.5%, most preferably more than 94% homology to any of the sequences as represented in SEQ ID NO 159 or 161 (BE95 or BE96 sequences) in the region spanning positions 7932 to 8271 of the NS5B region as shown in Figure 1.

Preferentially the above-mentioned genomic HCV sequences depict sequences from the coding regions of all the above-mentioned sequences.

According to the nucleotide distance classification system (with said nucleotide distances being calculated as explained above), said sequences of said composition are selected from:

- a nucleotide distance of less than 0.53, preferably less than 0.51, more preferably less than 0.49 for the E1 region to the type 5 sequences depicted above;
- a nucleotide distance of less than 0.3, preferably less than 0.28, more preferably of less than 0.26 for the Core region to the type 5 sequences depicted above;
- a nucleotide distance of less than 0.072, preferably less than 0.071, more preferably less than 0.070 for the NS5B region to the type 5 sequences as depicted above.

Isolates with similar sequences in the 5'UR to a group of isolates including SA1, SA3, and SA7 described in the 5'UR by Bukh et al. (1992), have been reported and described in the 5'UR and NS5 region as group V by Cha et al. (1992; WO 92/19743). This group of isolates belongs to type 5a as described in the present invention (SEQ ID NO 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 151, 153, 155, 157, 159, 161, 197 and 199).

Also included within the present invention are sequence variants of the polynucleic acids as selected from any of the nucleotide sequences as given in any of the above given SEQ ID numbers with said sequence variants containing either deletion and/or insertions of one or more nucleotides, mainly at the extremities of oligonucleotides (either 3' or 5'), or substitutions of some non-essential nucleotides (i.e. nucleotides not essential to discriminate between different genotypes of HCV) by others (including modified nucleotides an/or inosine), for example, a type 1 or 2 sequence might be modified into a type 5 sequence by replacing some nucleotides of the type 1 or 2 sequence with type-specific nucleotides of type 5 as shown in Figure 3 (Core region), Figure 4 (Core/E1 region), Figure 10 (NS3 / NS4 region), Figure 14 (E1/E2 region).

Another group of isolates including BU74 and BU79 having similar sequences in the 5'UR to isolates including Z6 and Z7 as described in the 5'UR by Bukh et al. (1992), have been described in the 5'UR and classified as a new type 4 by the inventors of this application (Stuyver et al., 1993). Coding sequences, including core, E1 and NS5 sequences of several new Gabonese isolates belonging to this group, are disclosed in the present invention (SEQ ID NO 106, 108, 110, 112, 114, 116, 118, 120 and 122).

According to yet another embodiment, the present invention relates to a composition as defined above, wherein said polynucleic acids correspond to a nucleotide sequence selected from any of the following HCV type 4 genomic sequences:

- an HCV genomic sequence having a homology of more than 66%, preferably more than 68%, most preferably more than 70% homology in the E1 region spanning positions 574 to 957 to any of the sequences as represented in SEQ ID NO 118, 120 or 122 (GB358. GB549, GB809 sequences) as shown in Figure 4;
- an HCV genomic sequence having a homology of more than 71%, preferably more than 72%, most preferably more than 74% homology to any of the sequences as represented in SEQ ID NO 118, 120 or 122 (GB358, GB549, GB809 sequences) in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence having a homology of more than 92%, preferably more than 93%, most preferably more than 94% homology to any of the sequences as represented in SEQ ID NO 163 or 165 (GB809, CAM600 sequences) in the region spanning positions 1 to 378 of the Core/E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4c) having a homology of more than 85%, preferably more than 86%, more preferably more than 86.5% homology, most preferably more than 87, more than 88 or more than 89% homology to any of the sequences as represented in SEQ ID NO 183, 185 or 187 (GB116, GB215, GB809 sequences) in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4a) having a homology of more than 81%, preferably more than 83%, most preferably more than 85% homology to the sequence as represented in SEQ ID NO 189 (GB908 sequence) in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4e) having a homology of more than 85%, preferably more than 87%, most preferably more than 89% homology to any of the sequences as represented in SEQ ID NO 167 or 169 (CAM600, GB908 sequences) in the region

spanning positions 379 to 957 of the El region as shown in Figure 4;

- an HCV genomic sequence (subtype 4f) having a homology of more than 79%, preferably more than 81%, most preferably more than 83% homology to any of the sequences as represented in SEQ ID NO 171 or 173 (CAMG22, CAMG27 sequences) in the region spanning positions 379 to 957 of the EI region as shown in Figure 4;
- an HCV genomic sequence (subtype 4g) having a homology of more than 84%, preferably more than 86%, most preferably more than 88% homology to the sequence as represented in SEQ ID NO 175 (GB549 sequence) in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4h) having a homology of more than 83%, preferably more than 85%, most preferably more than 87% homology to the sequence as represented in SEQ ID NO 177 (GB438 sequence) in the region spanning positions 379 to 957 of the El region as shown in Figure 4;
- an HCV genomic sequence (subtype 4i) as having a homology of more than 76%, preferably more than 78%, most preferably more than 80% homology to the sequence as represented in SEQ ID NO 179 (CAR4/1205 sequence) in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4j?) having a homology of more than 84%, preferably more than 86%, most preferably more than 88% homology to the sequence as represented in SEQ ID NO 181 (CAR4/901 sequence) in the region spanning positions 379 to 957 of the E1 region as shown in figure 4;
- an HCV genomic sequence as having a homology of more than 73%, preferably more than 75%, most preferably more than 77% homology to any of the sequences as represented in SEQ ID NO 106, 108, 110, 112, 114, or 116 (GB48, GB116, GB215, GB358, GB549, GB809 sequences) in the region spanning positions 7932 to 8271 of the NS5 region as shown in figure 1;
- an HCV genomic sequence (subtype 4c) having a homology of more than 88%, preferably more than 89%, most preferably more than 90% homology to any of the sequences as represented in SEQ ID NO 106, 108, 110, or 112 (GB48, GB116, GB215, GB358 sequences) in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1:
- an HCV genomic sequence (subtype 4e) having a homology of more than 88%, preferably more than 89%, most preferably more than 90% homology to any of the sequences as

represented in SEQ ID NO 116 or 201 (GB809 or CAM 600 sequences) in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1;

- an HCV genomic sequence (subtype 4f) having a homology of more than 87%, preferably more than 89%, most preferably more than 90% homology to the sequence as represented in SEQ ID NO 203 (CAMG22 sequence) in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence (subtype 4g) as having a homology of more than 85%, preferably more than 87%, most preferably more than 89% homology to the sequence as represented in SEQ ID NO 114 (GB549 sequence) in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence (subtype 4h) as having a homology of more than 86%, preferably more than 87%, more preferably more than 88% homology, more preferably more than 89% homology to the sequence as represented in SEQ ID NO 207 (GB437 sequence) in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence (subtype 4i) having a homology of more than 84%, preferably more than 86%, most preferably more than 88% homology to the sequence as represented in SEQ ID NO 209 (CAR4/1205 sequence) in the region spanning positions 7932 to 8271 of the NS5 region as shown in figure 1;
- an HCV genomic sequence (subtype 4j) having a homology of more than 81%, preferably more than 83%, most preferably more than 85% homology to the sequence as represented in SEQ ID NO 211 (CAR1/501 sequence) in the region spanning positions 7932 to 8271 of the NS5 region as shown in figure 1.

Preferentially the above-mentioned genomic HCV sequences depict sequences from the coding regions of all the above-mentioned sequences.

According to the nucleotide distance classification system (with said nucleotide distances being calculated as explained above), said sequences of said composition are selected from:

- an HCV genomic sequence (type 4) being characterized as having a nucleotide distance of less than 0.52, 0.50, 0.4880, 0.46, 0.44, 0.43 or most preferably less than 0.42 in the region spanning positions 574 to 957 to any of the sequences as represented in SEQ ID NO 118, 120 or 122 in the region spanning positions 1 to 957 of the Core/E1 region as shown in Figure 4;
- an HCV genomic sequence (type 4) being characterized as having a nucleotide distance of

less than 0.39, 0.36 0.34 0.32 or most preferably less than 0.31 to any of the sequences as represented in SEQ ID NO 118, 120 or 122 in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;

- an HCV genomic sequence (subtype 4c) being characterized as having a nucleotide distance of less than 0.27, 0.26, 0.24, 0.22, 0.20, 0.18, 0.17, 0.162, 0.16 or most preferably less than 0.15 to any of the sequences as represented in SEQ ID NO 183, 185 or 187 in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4a) being characterized as having a nucleotide distance of less than 0.30, 0.28, 0.26, 0.24, 0.22, 0.21 or most preferably of less than 0.205 to the sequence as represented in SEQ ID NO 189 in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4e) being characterized as having a nucleotide distance of less than 0.26, 0.25, 0.23, 0.21, 0.19, 0.17, 0.165, most preferably less than 0.16 to any of the sequences as represented in SEQ ID NO 167 or 169 in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4f) being characterized as having a nucleotide distance of less than 0.26, 0.24, 0.22, 0.20, 0.18, 0.16, 0.15 or most preferably less than 0.14 to any of the sequences as represented in SEQ ID NO 171 or 173 in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4g) being characterized as having a nucleotide distance of less than 0.20, 0.19, 0.18, 0.17 or most preferably of less than 0.16 to the sequence as represented in SEQ ID NO 175 in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4h) being characterized as having a nucleotide distance of less than 0.20, 0.19, 0.18, 0.17 and most preferably of less than 0.16 to the sequence as represented in SEQ ID NO 177 in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4i) being characterized as having a nucleotide distance of less than 0.27, 0.25, 0.23, 0.21 and preferably less than 0.16 to the sequence as represented in SEQ ID NO 179 in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4j?) being characterized as having a nucleotide distance of less than 0.19, 0.18, 0.17, 0.165 and most preferably of less than 0.16 to the

- sequence as represented in SEQ ID NO 181 in the region spanning positions 379 to 957 of the E1 region as shown in figure 4;
- an HCV genomic sequence (type 4) being characterized as having a nucleotide distance of less than 0.35, 0.34, 0.32 and most preferably of less than 0.30 to any of the sequences as represented in SEQ ID NO 106, 108, 110, 112, 114, or 116 in the region spanning positions 7932 to 8271 of the NS5 region as shown in figure 1;
- an HCV genomic sequence (subtype 4c) being characterized as having a nucleotide distance of less than 0.18, 0.16, 0.14, 0.135, 0.13, 0.1275 or most preferably less than 0.125 to any of the sequences as represented in SEQ ID NO 106, 108, 110, or 112 in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence (subtype 4e) being characterized as having a nucleotide distance of less than 0.15, 0.14, 0.135, 0.13 and most preferably of less than 0.125 to any of the sequences as represented in SEQ ID NO 116 or 201 in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence (subtype 4f) being characterized as having a nucleotide distance of less than 0.15, 0.14, 0.135, 0.13 or most preferably less than 0.125 to the sequence as represented in SEQ ID NO 203 in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence (subtype 4g) being characterized as having a nucleotide distance of less than 0.17, 0.16, 0.15, 0.14, 0.13 or most preferably less than 0.125 to the sequence as represented in SEQ ID NO 114 in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence (subtype 4h) being characterized as having a nucleotide distance of less than 0.155, 0.15, 0.145, 0.14, 0.135, 0.13 or most preferably less than 0.125 to the sequence as represented in SEQ ID NO 207 in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence (subtype 4i) being characterized as having a nucleotide distance of less than 0.17, 0.16, 0.15, 0.14, 0.13 or most preferably of less than 0.125 to the sequence as represented in SEQ ID NO 209 in the region spanning positions 7932 to 8271 of the NS5 region as shown in figure 1;
- an HCV genomic sequence (subtype 4j) being characterized as having a nucleotide distance of less than 0.21, 0.20, 0.19, 0.18, 0.17, 0.16, 0.15, 0.14, 0.13 and most preferably of less than 0.125 to the sequence as represented in SEQ ID NO 211 in the region spanning

positions 7932 to 8271 of the NS5 region as shown in figure 1.

Also included within the present invention are sequence variants of the polynucleic acids as selected from any of the nucleotide sequences as given in any of the above given SEQ ID numbers with said sequence variants containing either deletion and/or insertions of one or more nucleotides, mainly at the extremities of oligonucleotides (either 3' or 5'), or substitutions of some non-essential nucleotides (i.e. nucleotides not essential to discriminate between different genotypes of HCV) by others (including modified nucleotides an/or inosine), for example, a type 1 or 2 sequence might be modified into a type 4 sequence by replacing some nucleotides of the type 1 or 2 sequence with type-specific nucleotides of type 4 as shown in Figure 3 (Core region), Figure 4 (Core/E1 region), Figure 10 (NS3 / NS4 region), Figure 14 (E1/E2 region).

The present invention also relates to a sequence as represented in SEQ ID NO 193 (GB724 sequence).

After aligning NS5 or E1 sequences of GB48, GB, 116, GB215, GB358, GB549 and GB809, these isolates clearly segregated into 3 subtypes within type 4: GB48, GB116, GB215 and GB358 belong to the sybtype designated 4c, GB549 to subtype 4g and GB809 to subtype 4e. In NS5, GB809 (subtype 4e) showed a higher nucleic acids homology to subtype 4c isolates (85.6 - 86.8%) than to GB549 (subtype 4g, 79.7%), while GB549 showed similar homologies to both other subtypes (78.8 to 80% to subtype 4c and 79.7% to subtype 4e). In E1, subtype 4c showed equal nucleic acid homologies of 75.2% to subtypes 4g and 4e while 4g and 4e were 78.4% homologous. At the amino acid level however, subtype 4e showed a normal homology to subtype 4c (80.2%), while subtype 4g was more homologous to 4c (83.3%) and 4e (84.1%).

According to yet another embodiment, the present invention relates to a composition as defined above, wherein said polynucleic acids correspond to a nucleotide sequence selected from any of the following HCV type 2d genomic sequences:

- an HCV genomic sequence as having a homology of more than 78%, preferably more than 80%, most preferably more than 82% homology to the sequence as represented in SEQ ID NO (NE92) 143 in the region spanning positions 379 to 957 of the Core/E1 region as shown in Figure 4;
- an HCV genomic sequence as having a homology of more than 74%, preferably more than 76%, most preferably more than 78% homology to the sequence as represented in SEQ ID NO 143 (NE92) in the region spanning positions 574 to 957 as shown in Figure 4;

- an HCV genomic sequence as having a homology of more than 87%, preferably more than 89%, most preferably more than 91% homology to the sequence as represented in SEQ ID NO 145 (NE92) in the region spanning positions 7932 to 8271 of the NS5B region as shown in Figure 1.

Preferentially the above-mentioned genomic HCV sequences depict sequences from the coding regions of all the above-mentioned sequences.

According to the nucleotide distance classification system (with said nucleotide distances being calculated as explained above), said sequences of said composition are selected from:

- a nucleotide distance of less than 0.32, preferably less than 0.31, more preferably less than 0.30 for the E1 region (574 to 957) to any of the above specified sequences:
- a nucleotide distance of less than 0.08, preferably less than 0.07, more preferably less than 0.06 for the Core region (1 to 378) to any of the above given sequences
- a nucleotide distance of less than 0.15, preferentially less than 0.13, more preferentially less than 0.12 for the NS5B region to any of the above-specified sequences.

Polynucleic acid sequences according to the present invention which are homologous to the sequences as represented by a SEQ ID NO can be characterized and isolated according to any of the techniques known in the art, such as amplification by means of type or subtype specific primers, hybridization with type or subtype specific probes under more or less stringent conditions, serological screening methods (see examples 4 and 11) or via the LiPA typing system.

Polynucleic acid sequences of the genomes indicated above from regions not yet depicted in the present examples, figures and sequence listing can be obtained by any of the techniques known in the art, such as amplification techniques using suitable primers from the type or subtype specific sequences of the present invention.

The present invention relates also to a composition as defined above, wherein said polynucleic acid is liable to act as a primer for amplifying the nucleic acid of a certain isolate belonging to the genotype from which the primer is derived.

An example of a primer according to this embodiment of the invention is HCPr 152 as shown in table 7 (SEO ID NO 79).

The term "primer" refers to a single stranded DNA oligonucleotide sequence capable of acting as a point of initiation for synthesis of a primer extension product which is complementary to the nucleic acid strand to be copied. The length and the sequence of the primer must be such that they allow to prime the synthesis of the extension products.

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Preferably the primer is about 5-50 nucleotides. Specific length and sequence will depend on the complexity of the required DNA or RNA targets, as well as on the conditions of primer use such as temperature and ionic strength.

The fact that amplification primers do not have to match exactly with corresponding template sequence to warrant proper amplification is amply documented in the literature (Kwok et al., 1990).

The amplification method used can be either polymerase chain reaction (PCR; Saiki et al., 1988), ligase chain reaction (LCR; Landgren et al., 1988; Wu & Wallace, 1989; Barany, 1991), nucleic acid sequence-based amplification (NASBA; Guatelli et al., 1990; Compton. 1991), transcription-based amplification system (TAS; Kwoh et al., 1989), strand displacement amplification (SDA; Duck, 1990; Walker et al., 1992) or amplification by means of Qß replicase (Lizardi et al., 1988; Lomeli et al., 1989) or any other suitable method to amplify nucleic acid molecules using primer extension. During amplification, the amplified products can be conveniently labelled either using labelled primers or by incorporating labelled nucleotides. Labels may be isotopic (32P, 35S, etc.) or non-isotopic (biotin, digoxigenin, etc.). The amplification reaction is repeated between 20 and 80 times. advantageously between 30 and 50 times.

The present invention also relates to a composition as defined above, wherein said polynucleic acid is able to act as a hybridization probe for specific detection and/or classification into types of a nucleic acid containing said nucleotide sequence, with said oligonucleotide being possibly labelled or attached to a solid substrate.

The term "probe" refers to single stranded sequence-specific oligonucleotides which have a sequence which is complementary to the target sequence of the HCV genotype(s) to be detected.

Preferably, these probes are about 5 to 50 nucleotides long, more preferably from about 10 to 25 nucleotides.

The term "solid support" can refer to any substrate to which an oligonucleotide probe can be coupled, provided that it retains its hybridization characteristics and provided that the background level of hybridization remains low. Usually the solid substrate will be a microtiter plate, a membrane (e.g. nylon or nitrocellulose) or a microsphere (bead). Prior to application to the membrane or fixation it may be convenient to modify the nucleic acid probe in order to facilitate fixation or improve the hybridization efficiency. Such modifications may encompass homopolymer tailing, coupling with different reactive groups such as aliphatic

groups, NH₂ groups, SH groups, carboxylic groups, or coupling with biotin or haptens.

The present invention also relates to the use of a composition as defined above for detecting the presence of one or more HCV genotypes, more particularly for detecting the presence of a nucleic acid of any of the HCV genotypes having a nucleotide sequence as defined above, present in a biological sample liable to contain them, comprising at least the following steps:

- (i) possibly extracting sample nucleic acid,
- (ii) possibly amplifying the nucleic acid with at least one of the primers as defined above or any other HCV subtype 2d, HCV type 3, HCV type 4, HCV type 5 or universal HCV primer,
- (iii) hybrizing the nucleic acids of the biological sample, possibly under denatured conditions, and with said nucleic acids being possibly labelled during or after amplification, at appropriate conditions with one or more probes as defined above, with said probes being preferably attached to a solid substrate,
- (iv) washing at appropriate conditions,
- (v) detecting the hybrids formed,
- (vi) inferring the presence of one or more HCV genotypes present from the observed hybridization pattern.

Preferably, this technique could be performed in the Core or NS5B region.

The term "nucleic acid" can also be referred to as analyte strand and corresponds to a single- or double-stranded nucleic acid molecule. This analyte strand is preferentially positive-or negative stranded RNA, cDNA or amplified cDNA.

The term "biological sample" refers to any biological sample (tissue or fluid) containing HCV nucleic acid sequences and refers more particularly to blood serum or plasma samples.

The term "HCV subtype 2d primer" refers to a primer which specifically amplifies HCV subtype 2d sequences present in a sample (see Examples section and figures).

The term "HCV type 3 primer" refers to a primer which specifically amplifies HCV type 3 sequences present in a sample (see Examples section and figures).

The term "HCV type 4 primer" refers to a primer which specifically amplifies HCV type 4 genomes present in a sample.

The term "universal HCV primer" refers to oligonucleotide sequences complementary to any of the conserved regions of the HCV genome.

The term "HCV type 5 primer" refers to a primer which specifically amplifies HCV type

5 genomes present in a sample. The term "universal HCV primer" refers to oligonucleotide sequences complementary to any of the conserved regions of the HCV genome.

The expression "appropriate" hybridization and washing conditions are to be understood as stringent and are generally known in the art (e.g. Maniatis et al., Molecular Cloning: A Laboratory Manual, New York, Cold Spring Harbor Laboratory, 1982).

However, according to the hybridization solution (SSC, SSPE, etc.), these probes should be hybridized at their appropriate temperature in order to attain sufficient specificity.

The term "labelled" refers to the use of labelled nucleic acids. This may include the use of labelled nucleotides incorporated during the polymerase step of the amplification such as illustrated by Saiki et al. (1988) or Bej et al. (1990) or labelled primers, or by any other method known to the person skilled in the art.

The process of the invention comprises the steps of contacting any of the probes as defined above, with one of the following elements:

- either a biological sample in which the nucleic acids are made available for hybridization,
- or the purified nucleic acids contained in the biological sample
- or a single copy derived from the purified nucleic acids,
- or an amplified copy derived from the purified nucleic acids, with said elements or with said probes being attached to a solid substrate.

The expression "inferring the presence of one or more HCV genotypes present from the observed hybridization pattern" refers to the identification of the presence of HCV genomes in the sample by analyzing the pattern of binding of a panel of oligonucleotide probes. Single probes may provide useful information concerning the presence or absence of HCV genomes in a sample. On the other hand, the variation of the HCV genomes is dispersed in nature, so rarely is any one probe able to identify uniquely a specific HCV genome. Rather, the identity of an HCV genotype may be inferred from the pattern of binding of a panel of oligonucleotide probes, which are specific for (different) segments of the different HCV genomes. Depending on the choice of these oligonucleotide probes, each known HCV genotype will correspond to a specific hybridization pattern upon use of a specific combination of probes. Each HCV genotype will also be able to be discriminated from any other HCV genotype amplified with the same primers depending on the choice of the oligonucleotide probes. Comparison of the generated pattern of positively hybridizing probes for a sample containing one or more unknown HCV sequences to a scheme of expected

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hybridization patterns, allows one to clearly infer the HCV genotypes present in said sample.

The present invention thus relates to a method as defined above, wherein one or more hybridization probes are selected from any of SEQ ID NO 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59 or 61, 106, 108, 110, 112, 114, 116, 118, 120, 122, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 198, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 222, 269 or sequence variants thereof, with said sequence variants containing deletions and/or insertions of one or more nucleotides, mainly at their extremities (either 3' or 5'), or substitutions of some non-essential nucleotides (i.e. nucleotides not essential to discriminate between genotypes) by others (including modified nucleotides or inosine), or with said variants consisting of the complement of any of the above-mentioned oligonucleotide probes, or with said variants consisting of ribonucleotides instead of deoxyribonucleotides, all provided that said variant probes can be caused to hybridize with the same specificity as the oligonucleotide probes from which they are derived.

In order to distinguish the amplified HCV genomes from each other, the target polynucleic acids are hybridized to a set of sequence-specific DNA probes targetting HCV genotypic regions located in the HCV polynucleic acids.

Most of these probes target the most type-specific regions of HCV genotypes, but some can be caused to hybridize to more than one HCV genotype.

According to the hybridization solution (SSC, SSPE, etc.), these probes should be stringently hybridized at their appropriate temperature in order to attain sufficient specificity. However, by slightly modifying the DNA probes, either by adding or deleting one or a few nucleotides at their extremities (either 3' or 5'), or substituting some non-essential nucleotides (i.e. nucleotides not essential to discriminate between types) by others (including modified nucleotides or inosine) these probes or variants thereof can be caused to hybridize specifically at the same hybridization conditions (i.e. the same temperature and the same hybridization solution). Also changing the amount (concentration) of probe used may be beneficial to obtain more specific hybridization results. It should be noted in this context, that probes of the same length, regardless of their GC content, will hybridize specifically at approximately the same temperature in TMACl solutions (Jacobs et al., 1988).

Suitable assay methods for purposes of the present invention to detect hybrids formed between the oligonucleotide probes and the nucleic acid sequences in a sample may comprise

any of the assay formats known in the art, such as the conventional dot-blot format, sandwich hybridization or reverse hybridization. For example, the detection can be accomplished using a dot blot format, the unlabelled amplified sample being bound to a membrane, the membrane being incorporated with at least one labelled probe under suitable hybridization and wash conditions, and the presence of bound probe being monitored.

An alternative and preferred method is a "reverse" dot-blot format, in which the amplified sequence contains a label. In this format, the unlabelled oligonucleotide probes are bound to a solid support and exposed to the labelled sample under appropriate stringent hybridization and subsequent washing conditions. It is to be understood that also any other assay method which relies on the formation of a hybrid between the nucleic acids of the sample and the oligonucleotide probes according to the present invention may be used.

According to an advantageous embodiment, the process of detecting one or more HCV genotypes contained in a biological sample comprises the steps of contacting amplified HCV nucleic acid copies derived from the biological sample, with oligonucleotide probes which have been immobilized as parallel lines on a solid support.

According to this advantageous method, the probes are immobilized in a Line Probe Assay (LiPA) format. This is a reverse hybridization format (Saiki et al., 1989) using membrane strips onto which several oligonucleotide probes (including negative or positive control oligonucleotides) can be conveniently applied as parallel lines.

The invention thus also relates to a solid support, preferably a membrane strip, carrying on its surface, one or more probes as defined above, coupled to the support in the form of parallel lines.

The LiPA is a very rapid and user-friendly hybridization test. Results can be read 4 h. after the start of the amplification. After amplification during which usually a non-isotopic label is incorporated in the amplified product, and alkaline denaturation, the amplified product is contacted with the probes on the membrane and the hybridization is carried out for about 1 to 1,5 h hybridized polynucleic acid is detected. From the hybridization pattern generated, the HCV type can be deduced either visually, but preferably using dedicated software. The LiPA format is completely compatible with commercially available scanning devices, thus rendering automatic interpretation of the results very reliable. All those advantages make the LiPA format liable for the use of HCV detection in a routine setting. The LiPA format should be particularly advantageous for detecting the presence of different HCV genotypes.

The present invention also relates to a method for detecting and identifying novel HCV

genotypes, different from the known HCV genomes, comprising the steps of:

- determining to which HCV genotype the nucleotides present in a biological sample belong, according to the process as defined above,
- in the case of observing a sample which does not generate a hybridization pattern compatible with those defined in Table 3, sequencing the portion of the HCV genome sequence corresponding to the aberrantly hybridizing probe of the new HCV genotype to be determined.

The present invention also relates to the use of a composition as defined above, for detecting one or more genotypes of HCV present in a biological sample liable to contain them, comprising the steps of:

- (i) possibly extracting sample nucleic acid,
- (ii) amplifying the nucleic acid with at least one of the primers as defined above,
- (iii) sequencing the amplified products
- (iv) inferring the HCV genotypes present from the determined sequences by comparison to all known HCV sequences.

The present invention also relates to a composition consisting of or comprising at least one peptide or polypeptide comprising a contiguous sequence of at least 5 amino acids corresponding to a contiguous amino acid sequence encoded by at least one of the HCV genomic sequences as defined above, having at least one amino acid differing from the corresponding region of known HCV (type 1 and/or type 2 and/or type 3) polyprotein sequences as shown in Table 3, or muteins thereof.

It is to be noted that, at the level of the amino acid sequence, an amino acid difference (with respect to known HCV amino acid sequences) is necessary, which means that the polypeptides of the invention correspond to polynucleic acids having a nucleotide difference (with known HCV polynucleic acid sequences) involving an amino acid difference.

The new amino acid sequences, as deduced from the disclosed nucleotide sequences (see SEQ ID NO 1 to 62 and 106 to 123 and 143 to 218, 223 and 270), show homologies of only 59.9 to 78% with prototype sequences of type 1 and 2 for the NS4 region, and of only 53.9 to 68.8% with prototype sequences of type 1 and 2 for the E1 region. As the NS4 region is known to contain several epitopes, for example characterized in patent application EP-A-0 489 968, and as the E1 protein is expected to be subject to immune attack as part of the viral envelope and expected to contain epitopes, the NS4 and E1 epitopes of the new type 3, 4 and 5 isolates will consistently differ from the epitopes present in type 1 and 2 isolates. This is

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examplified by the type-specificity of NS4 synthetic peptides as presented in example 4, and the type-specificity of recombinant E1 proteins in example 11.

After aligning the new subtype 2d, type 3, 4 and 5 (see SEQ ID NO 1 to 62 and 106 to 123 and 143 to 218, 223 and 270) amino acid sequences with the prototype sequences of type 1a, 1b, 2a, and 2b, type- and subtype-specific variable regions can be delineated as presented in Figure 5 and 7.

As to the muteins derived from the polypeptides of the invention, Table 4 gives an overview of the amino acid substitutions which could be the basis of some of the muteins as defined above.

The peptides according to the present invention contain preferably at least 5 contiguous HCV amino acids, preferably however at least 8 contiguous amino acids, at least 10 or at least 15 (for instance at least 9, 11, 12, 13, 14, 20 or 25 amino acids) of the new HCV sequences of the invention.

TABLE 4

Amino acids	Synonymous groups Ser, Thr. Gly. Asn	
Ser (S)		
Arg (R)	Arg, His, Lys, Glu, Gln	
Leu (L)	Leu; Ile, Met, Phe, Val, Tyr	
Pro (P)	Pro, Ala, Thr, Gly	
Thr (T)	Thr, Pro, Ser, Ala, Gly, His, Gln	
Ala (A)	Ala, Pro, Gly, Thr	
Val (V)	Val, Met, Ile, Tyr, Phe, Leu, Val	
Gly (G)	Gly, Ala, Thr, Pro, Ser	
Ile (I)	Ile, Met, Leu, Phe, Val, Ile, Tyr	
Phe (F)	Phe, Met, Tyr, Ile, Leu, Trp, Val	
Tyr (Y)	Tyr, Phe, Trp, Met, Ile, Val, Leu	
Cys (C)	Cys, Ser, Thr, Met	
His (H)	His, Gln, Arg, Lys, Glu, Thr	
Gln (Q)	Gln, Glu, His, Lys, Asn, Thr, Arg	
Asn (N)	Asn, Asp. Ser, Gln	
Lys (K)	Lys, Arg, Glu, Gln, His	
Asp (D)	Asp, Asn, Giu, Gln	
Glu (E)	Glu, Gln, Asp, Lys, Asn, His, Arg	
Met (M)	Met, Ile, Leu, Phe, Val	

The polypeptides of the invention, and particularly the fragments, can be prepared by classical chemical synthesis.

The synthesis can be carried out in homogeneous solution or in solid phase.

For instance, the synthesis technique in homogeneous solution which can be used is the one described by Houbenweyl in the book entitled "Methode der organischen chemie" (Method of organic chemistry) edited by E. Wunsh, vol. 15-I et II. THIEME, Stuttgart 1974.

The polypeptides of the invention can also be prepared in solid phase according to the methods described by Atherton and Shepard in their book entitled "Solid phase peptide synthesis" (IRL Press, Oxford, 1989).

The polypeptides according to this invention can be prepared by means of recombinant DNA techniques as described by Maniatis et al., Molecular Cloning: A Laboratory Manual, New York, Cold Spring Harbor Laboratory, 1982).

The present invention relates particularly to a polypeptide or peptide composition as defined above, wherein said contiguous sequence contains in its sequence at least one of the following amino acid residues:

L7, Q43, M44, S60, R67, Q70, T71, A79, A87, N106, K115, A127, A190, S130, V134, G142, I144, E152, A157, V158, P165, S177 or Y177, I178, V180 or E180 or F182, R184, I186, H187, T189, A190, S191 or G191, Q192 or L192 or I192 or V192 or E192, N193 or H193 or P193, W194 or Y194, H195, A197 or I197 or V197 or T197, V202, I203 or L203, Q208, A210, V212, F214, T216, R217 or D217 or E217 or V217, H218 or N218, H219 or V219 or L219, L227 or I227, M231 or E231 or Q231, T232 or D232 or A232 or K232, Q235 or I235, A237 or T237, I242, I246, S247, S248, V249, S250 or Y250, I251 or V251 or M251 or F251, D252, T254 or V254, L255 or V255, E256 or A256, M258 or F258 or V258, A260 or Q260 or S260, A261, T264 or Y264, M265, I266 or A266, A267, G268 or T268, F271 or M271 or V271, I277, M280 or H280, I284 or A284 or L84, V274, V291, N292 or S292, R293 or I293 or Y293, Q294 or R294, L297 or I297 or Q297, A299 or K299 or Q299, N303 or T303, T308 or L308, T310 or F310 or A310 or D310 or V310, L313, G317 or Q317, L333, S351, A358, A359, A363, S364, A366, T369, L373, F376, Q386, 1387, S392, I399, F402, I403, R405, D454, A461, A463, T464, K484, Q500, E501, S521, K522, H524, N528, S531, S532, V534, F536, F537, M539, I546, C1282, A1283, H1310, V1312, Q1321, P1368, V1372, V1373, K1405, Q1406, S1409, A1424, A1429, C1435, \$1436, \$1456, H1496, A1504, D1510, D1529, I1543, N1567, D1556, N1567, M1572, Q1579, L1581, S1583, F1585, V1595, E1606 or T1606, M1611, V1612 or L1612, P1630, C1636, P1651, T1656 or I1656, L1663, V1667, V1677, A1681, H1685, E1687, G1689, V1695, A1700, Q1704, Y1705, A1713, A1714 or S1714, M1718, D1719, A1721 or T1721, R1722, A1723 or V1723, H1726 or G1726, E1730, V1732, F1735, I1736, S1737, R1738, T1739, G1740, Q1741, K1742, Q1743, A1744, T1745, L1746, E1747 or K1747, I1749, A1750, T1751 or A1751, V1753, N1755, K1756, A1757, P1758, A1759, H1762, T1763, Y1764, P2645, A2647, K2650, K2653 or L2653, S2664, N2673, F2680, K2681, L2686. H2692, Q2695 or L2695 or I2695, V2712, F2715, V2719 or Q2719, T2722, T2724, S2725, R2726, G2729, Y2735, H2739, I2748, G2746 or I2746, I2748, P2752 or K2752, P2754 or T2754, T2757 or P2757,

with said notation being composed of a letter representing the amino acid residue by its oneletter code, and a number representing the amino acid numbering according to Kato et al., 1990 as shown in Table 1 (comparison with other isolates). See also the numbering in Figures 2, 5, 7, and 11 (alignment amino acid sequences).

Within the group of unique and new amino acid residues of the present invention, the following residues were found to be specific for the following types of HCV according to the

HCV classification system used in the present invention:

- Q208, R217, E231, I235, I246, T264, I266, A267, F271, K299, L2686, Q2719 which are specific for the HCV subtype 2d sequences of the present invention as shown in Fig. 5 and 2;
- Q43, S60, R67, F182, I186, H187, A190, S191, L192, W194, V202, L203, V219,
 Q231, D232, A237, T254, M280, Q299, T303, L308, and/or L313 which are specific for the Core/E1 region of HCV type 3 of the invention as shown in Fig. 5;
- D1556, Q1579, L1581, S1584, F1585, E1606, V1612, P1630, C1636, T1656,
 L1663, H1685, E1687, G1689, V1695, Y1705, A1713, A1714, A1721, V1723,
 H1726, R1738, Q1743, A1744, E1747, I1749, A1751, A1759 and/or H1762 which are specific for the NS3/4 region of HCV type 3 sequences of the invention as shown in Fig. 7;
- K2665, D2666, R2670 which are specific for the NS5B region of HCV type 3 of the invention as shown in Fig. 2;
- L7, A79, A127, S130, E152, V158, S177 or Y177, V180 or E180, R184, T189, Q192 or E192 or I192, N193 or H193, I197 or V197, I203, A210, V212, E217, H218, H219, L227, A232, V249, I251 or M251, D252, L255 or V255, E256, M258 or V258 or F258, A260 or Q260, M265, T268, V271, V274, M280, I284, N292 or S292, Q294, L297 or I297, T308, A310 or D310 or V310 or T310, and G317 which are specific for the core/E1 region of HCV type 4 sequences of the present invention as shown in Fig. 5;
- P2645, K2650, K2653, G2656, V2658, T2668, N2673 or N2673, K2681, H2686,
 D2691, L2692, Q2695 or L2695 or I2695, Y2704, V2712, F2715, V2719, I2722,
 S2725, G2729, Y2735, G2746 or I2746, P2752 or K2752, Q2753, P2754 or
 T2754, T2757 or P2757 which are specific for the NS5B region of the HCV type
 4 sequences of the present invention as shown in Fig. 2;
- M44, Q70, A87, N106, K115, V137, G142, P165, I178, F251, A299, N303, Q317 which are specific for the Core/E1 region of the HCV type 4 sequences of the present invention as shown in Fig. 5;
- L333, S351, A358, A359, A363, S364, A366, T369, L373, F376, Q386, I387, S392, I399, F102, I403, R405, D454, A461, A463, T464, K484, Q500, E501, S521, K522, H524, N528, S532, V534, F537, M539, I546 which are specific for

- the E1/E2 region of the HCV type 5 sequences of the present invention as shown in Fig. 12;
- C1282, A1283, V1312, Q1321, P1368, V1372, K1405, Q1406, S1409, A1424, A1429, C1435, S1436, S1456, H1496, A1504, D1510, D1529, I1543, N1567, M1572, V1595, T1606, M1611, L1612, I1656, V1667, A1681, A1700, A1713, S1714, M1718, D1719, T1721, R1722, A1723, G1726, F1735, I1736, S1737, T1739, G1740, K1742, T1745, L1746, K1747, A1750, V1753, N1755, A1757, D1758, T1763, and Y1764 which are specific for the NS3/NS4 region of HCV type 5 sequences of the invention as shown in Fig. 7;
- A2647, L2653, S2674, F2680, T2724, R2726, Y2730, H2739 which are specific for the NS5B region of the HCV type 5 sequences of the present invention as shown in Fig. 2:
- A256, P1631, V1677, Q1704, E1730, V1732, Q1741 and T1751 which are specific for the HCV type 3 and 5 sequences of the present invention as shown in Fig. 5 and 7;
- T71, A157, I227, T237, T240, Y250, V251, S260, M271, T2673, T2722, I2748 which are specific for the HCV type 3 and 4 sequences of the present invention as shown in Fig. 5 and 2,
- V192, Y194, A197, P249, S250, R294 which are specific for the HCV type 4 and . 5 sequences of the present invention as shown in Fig. 5;
- I293 which is specific for the HCV type 4 and subtype 2d sequence of the present invention as shown in Fig. 5;
- D217 and R294 which are specific for the HCV type 3, 4 and 5 sequences of the present invention as shown in Fig. 5;
- L192 which is specific for the HCV type 3 and subtype 2d sequences of the present invention as shown in Fig. 5;
- G191 and T197 which are specific for the HCV type 3, 4 and subtype 2d sequences of the present invention as shown in Fig. 5;
- K232 which is specific for the HCV subtype 2d en type 5 sequences of the present invention as shown in Fig. 5.

and with said notation being composed of a letter, unambiguously representing the amino acid by its one-letter code, and a number representing the amino acid numbering according to Kato et al., 1990 (see also Table 1 for comparison with other isolates), as well as Figure 2 (NS5)

region), Figure 5 (Core/E1 region), Figure 7 (NS3/NS4 region), Figure 12 (E1/E2 region). Some of the above-mentioned amino acids may be contained in type or subtype specific epitopes.

For example M231 (detected in type 5) refers to a methionine at position 231. A glutamine (Q) is present at the same position 231 in type 3 isolates, whereas this position is occupied by an arginine in type 1 isolates and by a lysine (K) or asparagine (N) in type 2 isolates (see Figure 5).

The peptide or polypeptide according to this embodiment of the invention may be possibly labelled, or attached to a solid substrate, or coupled to a carrier molecule such as biotin, or mixed with a proper adjuvant.

The variable region in the core protein (V-CORE in Fig. 5) has been shown to be useful for serotyping (Machida et al., 1992). The sequence of the disclosed type 5 sequence in this region shows type-specific features. The peptide from amino acid 70 to 78 shows the following unique sequence for the sequences of the present inevntion (see figure 5):

QPTGRSWGQ (SEQ ID NO 93)

RSEGRTSWAQ (SEQ ID NO 220)

and RTEGRTSWAQ (SEQ ID NO 221)

Another preferred V-Core spanning region is the peptide spanning positions 60 to 78 of subtype 3c with sequence:

SRRQPIPRARRTEGRSWAQ (SEQ ID NO 268)

Five type-specific variable regions (V1 to V5) can be identified after aligning E1 amino acid sequences of the 4 genotypes, as shown in Figure 5.

Region V1 encompasses amino acids 192 to 203, this is the amino-terminal 10 amino acids of the E1 protein. The following unique sequences as shown in Fig. 5 can be deduced:

LEWRNTSGLYVL (SEQ ID NO 83)

VNYRNASGIYHI (SEQ ID NO 126)

QHYRNISGIYHV (SEQ ID NO 127)

EHYRNASGIYHI (SEQ ID NO 128)

IHYRNASGIYHI (SEQ ID NO 224)

VPYRNASGIYHV (SEQ ID NO 84)

VNYRNASGIYHI (SEQ ID NO 225)

VNYRNASGVYHI (SEQ ID NO 226)

VNYHNTSGIYHL (SEQ ID NO 227)

QHYRNASGIYHV (SEQ ID NO 228) QHYRNVSGIYHV (SEQ ID NO 229) IHYRNASDGYYI (SEQ ID NO 230) LQVKNTSSSYMV (SEQ ID NO 231)

Region V2 encompasses amino acids 213 to 223. The following unique sequences can be found in the V2 region as shown in Figure 5:

VYEADDVILHT (SEQ ID NO 85)

VYETEHHILHL (SEQ ID NO 129)

VYEADHHIMHL (SEQ ID NO 130)

VYETDHHILHL (SEQ ID NO 131)

VYEADNLILHA (SEQ ID NO 86)

VWQLRAIVLHV (SEQ ID NO 232)

VYEADYHILHL (SEQ ID NO 233)

VYETDNHILHL (SEQ ID NO 234)

VYETENHILHL (SEQ ID NO 235)

VFETVHHILHL (SEQ ID NO 236)

VFETEHHILHL (SEQ ID NO 237)

VFETDHHIMHL (SEQ ID NO 238)

VYETENHILHL (SEQ ID NO 239)

VYEADALILHA (SEQ ID NO 240)

Region V3 encompasses the amino acids 230 to 242. The following unique V3 region sequences can be deduced from Figure 5:

VQDGNTSTCWTPV (SEQ ID NO 87)

VQDGNTSACWTPV (SEQ ID NO 241)

VRVGNQSRCWVAL (SEQ ID NO 132)

VRTGNTSRCWVPL (SEQ ID NO 133)

VRAGNVSRCWTPV (SEQ ID NO 134)

EEKGNISRCWIPV (SEQ ID NO 242)

VKTGNQSRCWVAL (SEQ ID NO 243)

VRTGNQSRCWVAL (SEQ ID NO 244)

VKTGNQSRCWIAL (SEQ ID NO 245)

VKTGNVSRCWIPL (SEQ ID NO 247)

VKTGNVSRCWISL (SEQ ID NO 248)

VRKDNVSRCWVQI (SEQ ID NO 249)

Region V4 encompasses the amino acids 248 to 257. The following unique V4 region sequences can be deduced from figure 5:

VRYVGATTAS (SEQ ID NO 89)

APYIGAPLES (SEQ ID NO 135)

APYVGAPLES (SEQ ID NO 136)

AVSMDAPLES (SEQ ID NO 137)

APSLGAVTAP (SEQ ID NO 90)

APSFGAVTAP (SEQ ID NO 250)

VSQPGALTKG (SEQ ID NO 251)

VKYVGATTAS (SEQ ID NO 252)

APYIGAPVES (SEQ ID NO 253)

AQHLNAPLES (SEQ ID NO 254)

SPYVGAPLEP (SEQ ID NO 255)

SPYAGAPLEP (SEQ ID NO 256)

APYLGAPLEP (SEQ ID NO 257)

APYLGAPLES (SEQ ID NO 258)

APYVGAPLES (SEQ ID NO 259)

VPYLGAPLTS (SEQ ID NO 260)

APHLRAPLSS (SEQ ID NO 261)

APYLGAPLTS (SEQ ID NO 262)

Region V5 encompasses the amino acids 294 to 303. The following unique V5 region peptides can be deduced from figure 5:

RPRRHQTVQT (SEQ ID NO 91)

QPRRHWTTQD (SEQ ID NO 138)

RPRRHWTTQD (SEQ ID NO 139)

RPRQHATVQN (SEQ ID NO 92)

RPRQHATVQD (SEQ ID NO 263)

SPQHHKFVQD (SEQ ID NO 264)

RPRRLWTTQE (SEQ ID NO 265)

PPRIHETTQD (SEQ ID NO 266)

The variable region in the E2 region (HVR-2) of type 5a as shown in Figure 12 spanning amino acid positions 471 to 484 is also a preferred peptide according to the present invention

with the following sequence:

TISYANGSGPSDDK (SEQ ID NO 267)

The above given list of peptides are particularly suitable for vaccine and diagnostic development.

Also comprised in the present invention is any synthetic peptide or polypeptide containing at least 5 contiguous amino acids derived from the above-defined peptides in their peptidic chain.

According to a specific embodiment, the present invention relates to a composition as defined above, wherein said contiguous sequence is selected from any of the following HCV amino acid type 3 sequences:

- a sequence having a homology of more than 72%, preferably more than 74%, more preferably more than 77% and most preferably more than 80 or 84% homology to any of the amino acid sequences as represented in SEQ ID NO 14, 16, 18, 20, 22, 24, 26 or 28 (HD10, BR36, BR33 sequences) in the region spanning positions 140 to 319 in the Core/E1 region as shown in Figure 5;
- a sequence having a homology of more than 70%, preferably more than 72%, more preferably more than 75% homology, most preferably more than 81% homology to any of the amino acid sequences as represented in SEQ ID NO 14, 16, 18, 20, 22, 24, 26 or 28 (HD10, BR36, BR33 sequences) in the E1 region spanning positions 192 to 319 as shown in Figure 5;
- a sequence having a homology of more than 86%, preferably more than 88%, and most preferably more than 90% homology to the amino acid sequences as represented in SEQ ID NO 148 (type 3c); BE98 in the region spanning positions 1 to 110 in the Core region as shown in Figure 5;
- a sequence having a homology of more than 76%, preferably more than 78%, most preferably more than 80% to any of the amino acid sequences as represented in SEQ ID NO 30, 32, 34, 36, 38 or 40 (HCCl53, HD10, BR36 sequences) in the region spanning positions 1646 to 1764 in the NS3/NS4 region as shown in Figure 7 and 11;
- a sequence having a homology of more than 81%, preferably more than 83%, and most preferably more than 86% homology to any of the amino acid sequences as represented in SEQ ID NO 14, 16, 18, 20, 22, 24, 26 or 28 (HD10, BR36, BR33 sequences) in the region spanning positions 140 to 319 in the Core/E1 region as shown in Figure 5;
- a sequence having a homology of more than 81.5%, preferably more than 83%, and most

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preferably more than 86% homology to any of the amino acid sequences as represented in SEQ ID NO 14, 16, 18, 20, 22, 24, 26 or 28 (HD10, BR36, BR33 sequences) in the E1 region spanning positions 192 to 319 as shown in Figure 5;

- a sequence having a homology of more than 86%, preferably more than 88%, most preferably more than 90% to the amino acid sequence as represented in SEQ ID NO 150; (type 3c BE98) in the region spanning positions 2645 to 2757 in the NS5B region as shown in Figure 2.

According to yet another embodiment, the present invention relates to a composition as defined above, wherein said contiguous sequence is selected from any of the following HCV amino acid type 4 sequences:

- a sequence having a homology of more than 80%, preferably more than 82%, most preferably more than 84% homology to any of the amino acid sequences as represented in SEQ ID NO 118, 120, and 122 (GB358, GB549, GB809 sequences) in the region spanning positions 127 to 319 of the Core/E1 region as shown in Figure 5;
- a sequence having a homology of more than 73%, preferably more than 75%, most preferably more than 78% homology in the E1 region spanning positions 192 to 319 to any of the amino acid sequences as represented in SEQ ID NO 118, 120, and 122 (GB358, GB549, GB809 sequences) in the region spanning positions 140 to 319 of the Core/E1 region as shown in Figure 5;
- a sequence having more than 85%, preferably more than 86%, most preferably more than 87% homology to any of the amino acid sequences as represented in SEQ ID NO 118, 120 or 122 (GB358, GB549, GB809 sequences) in the region spanning positions 192 to 319 of E1 as shown in Figure 5;
- a sequence showing more than 73%, preferably more than 74%, most preferably more than 75% homology to any of the amino acid sequences as represented in SEQ ID NO 106, 108, 110, 112, 114 or 116 (GB48, GB116, GB215, GB358, GB549, GB809 sequences) in the region spanning positions 2645 to 2757 of the NS5B region as shown in Figure 2;
- a sequence having any of the sequences as represented in SEQ ID NO 164 or 166 (GB809 and CAM600 sequences) in the Core/E1 region as shown in Figure 5;
- a sequence having any of the sequences as represented in SEQ ID NO 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188 or 190 (CAM600, GB809, CAMG22, CAMG27, GB549, GB438, CAR4/1205, CAR4/901, GB116, GB215, GB958, GB809-4 sequences) in the E1 region as shown in Figure 5;

a sequence having any of the sequences as represented in SEQ ID NO 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212 (GB358, GB724, BE100, PC, CAM600, CAMG22, etc.) in the NS5B region.

The above-mentioned type 4 peptides polypeptides comprise at least an amino acid sequence selected from any HCV type 4 polyprotein with the exception of core sequence as disclosed by Simmonds et al. (1993, EG-29, see Figure 5).

According to yet another aspect, the present invention relates to a composition as defined above, wherein said contiguous sequence is selected from any of the following HCV amino acid type 5 sequences:

- a sequence having more than 93%, preferably more than 94%, most preferably more than 95% homology in the region spanning Core positions 1 to 191 to any of the amino acid sequences as represented in SEQ ID NO 42, 44, 46, 48, 50, 52 or 54 (PC sequences) and SEQ ID NO 152 (BE95) as shown in Figure 5;
- a sequence having more than 73%, preferably more than 74%, most preferably more than 76% homology in the region spanning E1 positions 192 to 319 to any of the amino acid sequences as represented in SEQ ID NO 42, 44, 46, 48, 50, 52 or 54 (PC sequences) as shown in Figure 5;
- a sequence having a more than 78%, preferably more than 80%, most preferably more than 83% homology to any of the amino acid sequences as represented in SEQ ID NO 42, 44, 46, 48, 50, 52, 54, 154, 156 (BE95, BE100) (PC sequences) in the region spanning positions 1 to 319 of the Core/E1 region as shown in Figure 5;
- a sequence having more than 90%, preferably more than 91%, most preferably more than 92% homology to any of the amino acid sequences represented in SEQ ID NO 56 to 58 (PC sequences) in the region spanning positions 1286 to 1403 of the NS3 region as shown in Figure 7 or 11;
- a sequence having more than 66%, more particularly 68%, most particularly 70% or more homology to any of the amino acid sequences as represented in SEQ ID NO 60 or 62 (PC sequences) in the region spanning positions 1646 to 1764 of the NS3/4 region as shown in Figure 7 or 11.

According to yet another embodiment, the present invention relates to a composition as defined above, wherein said contiguous sequence is selected from any of the following HCV amino acid type 2d sequences:

- a sequence having more than 83%, preferably more than 85%, most preferably more than

- 87% homology to the amino acid sequence as represented in SEQ ID NO 144 (NE92) in the region spanning positions 1 to 319 of the Core/E1 region as shown in Figure 5;
- a sequence having more than 79%, preferably more than 81%, most preferably more than 84% homology in the region spanning E1 positions 192 to 319 to the amino acid sequence as represented in SEQ ID NO 144 (NE92) as shown in Figure 12;
- a sequence having more than 95%, more particularly 96%, most particularly 97% or more homology to the amino acid sequence as represented in SEQ ID NO 146 (NE92) in the region spanning positions 2645 to 2757 of the NS5B region as shown in Figure 2.

The present invention also relates to a recombinant vector, particularly for cloning and/or expression, with said recombinant vector comprising a vector sequence, an appropriate prokaryotic, eukaryotic or viral promoter sequence followed by the nucleotide sequences as defined above, with said recombinant vector allowing the expression of any one of the HCV type 2 and/or HCV type 3 and/or type 4 and/or type 5 derived polypeptides as defined above in a prokaryotic, or eukaryotic host or in living mammals when injected as naked DNA, and more particularly a recombinant vector allowing the expression of any of the following HCV type 2d, type 3, type 4 or type 5 polypeptides spanning the following amino acid positions:

- a polypeptide starting at position 1 and ending at any position in the region between positions 70 and 326, more particularly a polypeptide spanning positions 1 to 70, 1 to 85, positions 1 to 120, positions 1 to 150, positions 1 to 191, positions 1 to 200, for expression of the Core protein, and a polypeptide spanning positions 1 to 263, positions 1 to 326, for expression of the Core and E1 protein;
- a polypeptide starting at any position in the region between positions 117 and 192, and ending at any position in the region between positions 263 and 326, for expression of E1, or forms that have the putative membrane anchor deleted (positions 264 to 293 plus or minus 8 amino acids);
 - a polypeptide starting at any position in the region between positions 1556 and 1688, and ending at any position in the region between positions 1739 and 1764, for expression of the NS4 regions, more particularly a polypeptide starting at position 1658 and ending at position 1711 for expression of the NS4a antigen, and more particularly, a polypeptide starting at position 1712 and ending between positions 1743 and 1972, for example 1712-1743, 1712-1764, 1712-1782, 1712-1972, 1712 to 1782 and 1902 to 1972 for expression of the NS4b protein or parts thereof.

The term "vector" may comprise a plasmid, a cosmid, a phage, or a virus.

In order to carry out the expression of the polypeptides of the invention in bacteria such as E. coli or in eukaryotic cells such as in S. cerevisiae, or in cultured vertebrate or invertebrate hosts such as insect cells, Chinese Hamster Ovary (CHO), COS, BHK, and MDCK cells, the following steps are carried out:

transformation of an appropriate cellular host with a recombinant vector, in which a nucleotide sequence coding for one of the polypeptides of the invention has been inserted under the control of the appropriate regulatory elements, particularly a promoter recognized by the polymerases of the cellular host and, in the case of a prokaryotic host, an appropriate ribosome binding site (RBS), enabling the expression in said cellular host of said nucleotide sequence. In the case of an eukaryotic host any artificial signal sequence or pre/pro sequence might be provided, or the natural HCV signal sequence might be employed, e.g. for expression of E1 the signal sequence starting between amino acid positions 117 and 170 and ending at amino acid position 191 can be used, for expression of NS4, the signal sequence starting between amino acid positions 1646 and 1659 can be used, culture of said transformed cellular host under conditions enabling the expression of said insert.

The present invention also relates to a composition as defined above, wherein said polypeptide is a recombinant polypeptide expressed by means of an expression vector as defined above.

The present invention also relates to a composition as defined above, for use in a method for immunizing a mammal, preferably humans, against HCV comprising administring a sufficient amount of the composition possibly accompanied by pharmaceutically acceptable adjuvants, to produce an immune response, more particularly a vaccine composition including HCV type 3 polypeptides derived from the Core, E1 or the NS4 region and/or HCV type 4 and/or HCV type 5 polypeptides and/or HCV type 2d polypeptides.

The present invention also relates to an antibody raised upon immunization with a composition as defined above by means of a process as defined above, with said antibody being reactive with any of the polypeptides as defined above, and with said antibody being preferably a monoclonal antibody.

The monoclonal antibodies of the invention can be produced by any hybridoma liable to be formed according to classical methods from splenic cells of an animal, particularly from

a mouse or rat, immunized against the HCV polypeptides according to the invention, or muteins thereof, or fragments thereof as defined above on the one hand, and of cells of a myeloma cell line on the other hand, and to be selected by the ability of the hybridoma to produce the monoclonal antibodies recognizing the polypeptides which has been initially used for the immunization of the animals.

The antibodies involved in the invention can be labelled by an appropriate label of the enzymatic, fluorescent, or radioactive type.

The monoclonal antibodies according to this preferred embodiment of the invention may be humanized versions of mouse monoclonal antibodies made by means of recombinant DNA technology, departing from parts of mouse and/or human genomic DNA sequences coding for H and L chains or from cDNA clones coding for H and L chains.

Alternatively the monoclonal antibodies according to this preferred embodiment of the invention may be human monoclonal antibodies. These antibodies according to the present embodiment of the invention can also be derived from human peripheral blood lymphocytes of patients infected with type 3, type 4 or type 5 HCV, or vaccinated against HCV. Such human monoclonal antibodies are prepared, for instance, by means of human peripheral blood lymphocytes (PBL) repopulation of severe combined immune deficiency (SCID) mice (for recent review, see Duchosal et al. 1992).

The invention also relates to the use of the proteins of the invention, muteins thereof, or peptides derived therefrom for the selection of recombinant antibodies by the process of repertoire cloning (Persson et al., 1991).

Antibodies directed to peptides derived from a certaing genotype may be used either for the detection of such HCV genotypes, or as therapeutic agents.

The present invention also relates to the use of a composition as defined above for incorporation into an immunoassay for detecting HCV, present in biological sample liable to contain it, comprising at least the following steps:

- (i) contacting the biological sample to be analyzed for the presence of HCV antibodies with any of the compositions as defined above preferably in an immobilized form under appropriate conditions which allow the formation of an immune complex, wherein said polypeptide can be a biotinylated polypeptide which is covalently bound to a solid substrate by means of streptavidin or avidin complexes,
- (ii) removing unbound components,
- (iii) incubating the immune complexes formed with heterologous antibodies, which

specifically bind to the antibodies present in the sample to be analyzed, with said heterologous antibodies having conjugated to a detectable label under appropriate conditions,

(iv) detecting the presence of said immunecomplexes visually or by means of densitometry and inferring the HCV serotype present from the observed hybridization pattern.

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The present invention also relates to the use of a composition as defined above, for incorporation into a serotyping assay for detecting one or more serological types of HCV present in a biological sample liable to contain it, more particularly for detecting E1 and NS4 antigens or antibodies of the different types to be detected combined in one assay format, comprising at least the following steps:

- (i) contacting the biological sample to be analyzed for the presence of HCV antibodies or antigens of one or more serological types, with at least one of the compositions as defined above, an immobilized form under appropriate conditions which allow the formation of an immunecomplex,
- (ii) removing unbound components,
- (iii) incubating the immunecomplexes formed with heterologous antibodies, which specifically bind to the antibodies present in the sample to be analyzed, with said heterologous antibodies having conjugated to a detectable label under appropriate conditions.
- (iv) detecting the presence of said immunecomplexes visually or by means of densitometry and inferring the presence of one or more HCV serological types present from the observed binding pattern.

The present invention also relates to the use of a composition as defined above, for immobilization on a solid substrate and incorporation into a reversed phase hybridization assay, preferably for immobilization as parallel lines onto a solid support such as a membrane strip, for determining the presence or the genotype of HCV according to a method as defined above.

The present invention thus also relates to a kit for determining the presence of HCV genotypes as defined above present in a biological sample liable to contain them, comprising:

- possibly at least one primer composition containing any primer selected from those defined above or any other HCV type 3 and/or HCV type 4, and/or HCV type 5. or universal HCV primers,

- at least one probe composition as defined above, with said probes being preferentially immobilized on a solid substrate, and more preferentially on one and the same membrane strip.
- a buffer or components necessary for producing the buffer enabling hybridization reaction between these probes and the possibly amplified products to be carried out,
- means for detecting the hybrids resulting from the preceding hybriziation,
- possibly also including an automated scanning and interpretation device for inferring the HCV genotypes present in the sample from the observed hybridization pattern.

The genotype may also be detected by means of a type-specific antibody as defined above, which is linked to any polynucleotide sequence that can afterwards be amplified by PCR to detect the immune complex formed (Immuno-PCR, Sano et al., 1992);

The present invention also relates to a kit for determining the presence of HCV antibodies as defined above present in a biological sample liable to contain them, comprising:

- at least one polypeptide composition as defined above, preferentially in combination with other polypeptides or peptides from HCV type 1, HCV type 2 or other types of HCV, with said polypeptides being preferentially immobilized on a solid substrate, and more preferentially on one and the same membrane strip,
- a buffer or components necessary for producing the buffer enabling binding reaction between these polypeptides and the antibodies against HCV present in the biological sample,
- means for detecting the immunecomplexes formed in the preceding binding reaction,
- possibly also including an automated scanning and interpretation device for inferring the HCV genotypes present in the sample from the observed binding pattern.

Figure Legends

Figure 1

Alignment of consensus nucleotide sequences for each of the type 3a isolates BR34, BR36, and BR33, deduced from the clones with SEQ ID NO 1, 5, 9; type 4 isolates GB48, GB116, GB215, GB358, GB549, GB809, CAM600, CAMG22, GB438, CAR4/1205, CAR1/501 (SEQ ID NO. 106, 108, 110, 112, 114, 116, 201, 203, 205, 207, 209 and 211); type 5a isolates BE95 and BE96 (SEQ ID NO 159 and 161) and type 2d isolate NE92 (SEQ ID NO 145) from the region between nucleotides 7932 and 8271, with known sequences from the corresponding region of isolates HCV-1, HCV-J, HC-J6, HC-J8, T1 and T9, and others as shown in Table 3.

Figure 2

Alignment of amino acids sequences deduced from the nucleic acid sequences as represented in Figure 1 from the subtype 3a clones BR34 (SEQ ID NO 2, 4), BR36 (SEQ ID NO 6, 8) and BR33 (SEQ ID NO 10, 12), the subtype 3c clone BE98 (SEQ ID NO 150), and the type 4 clones GB48 (SEQ ID NO 107), GB116 (SEQ ID NO 109), GB215 (SEQ ID NO 111), GB358 (SEQ ID NO 113), GB549 (SEQ ID NO 115) GB809 (SEQ ID NO 117); CAM600, CAMG22, GB438, CAR4/1205, CAR1/501 (SEQ ID NO 202, 204, 206, 208, 210, 212); the type 5a clones BE95 and BE96 (SEQ ID NO 160 and 162); as well as the subtype 2d isolate NE92 (SEQ ID NO 146) from the region between amino acids 2645 to 2757 with known sequences from the corresponding region of isolates HCV-I, HCV-J, HC-J6, and HC-J8, T1 and T9, and other sequences as shown in Table 3.

Figure 3

Alignment of type 2d, 3c, 4 and 5a nucleotide sequences from isolates NE92, BE98, GB358, GB809, CAM600, GB724, BE95 (SEQ ID NO 143, 147, 191, 163, 165, 193 and 151) in the Core region between nucleotide positions 1 and 500, with known sequences from the corresponding region of type 1, type 2, type 3 and type 4 sequences.

Figure 4

Alignment of nucleotide sequences for the subtype 2d isolate NE92 (SEQ ID NO 143), the type 4 isolates GB358 (SEQ ID NO 118 and 187), GB549 (SEQ ID NO 120 and 175), and

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GB809-2 (SEQ ID NO 122 and 169), GB 809-4, BG116, GB215, CAM600, CAMG22, CAMG27, GB438, CAR4/1205, CAR4/901 (SEQ ID NO 189, 183, 185, 167, 171, 173, 177, 179, 181), sequences for each of the subtype 3a isolates HD10, BR36, and BR33, (SEQ ID NO 13, 15, 17 (HD10), 19, 21 (BR36) and 23, 25 or 27 (BR23) and the subtype 5a isolates BE95 and BE100 (SEQ ID NO 143 and 195) from the region between nucleotides 379 and 957, with known sequences from the corresponding region of type 1 and 2 and 3.

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Figure 5

Alignment of amino acid sequences deduced from the new HCV nucleotide sequences of the Core/E1 region of isolates BR33, BR36, HD10, GB358, GB549, and GB809, PC or BE95, CAM600, and GB724 (SEQ ID NO. 14, 20, 24, 119 or 192, 121, 123 or 164, 54 or 152, 166 and 194) from the region between positions 1 and 319, with known sequences from type 1a (HCV-1), type 1b (HCV-J), type 2a (HC-JG), type 2b (HC-J8), NZL1, HCV-TR, positions 7-89 of type 3a (E-b1), and positions 8-88 of type 4a (EG-29). V-Core, variable region with type-specific features in the core protein, V1, variable region 1 of the E1 protein, V2, variable region 2 of the E1 protein, V3, variable region 3 of the E1 protein, V4, variable region 4 of the E1 protein, V5, variable region 5 of the E1 protein.

Figure 6

Alignment of nucleotide sequences of isolates HCCL53, HD10 and BR36, deduced from clones with SEQ ID NO 29, 31, 33, 35, 37 and 39, from the NS3/4 region between nucleotides 4664 to 5292, with known sequences from the corresponding region of isolates HCV-1, HCV-J, HC-J6, and HC-J8, EB1, EB2, EB6 and EB7.

Figure 7

Alignment of amino acid sequences deduced from the new HCV nucleotide sequences of the NS3/NS4 region of isolate BR36 (SEQ ID NO 36, 38 and 40) and BE95 (SEQ ID NO 270). NS4-1, indicates the region that was synthesized as synthetic peptide 1 of the NS4 region, NS4-5, indicates the region that was synthesized as synthetic peptide 5 of the NS4 region; NS4-7, indicates the region that was synthesized as synthetic peptide 7 of the NS4 region.

Figure 8

Reactivity of the three LIPA-selected (Stuyver et al., 1993) type 3 sera on the Inno-LIA HCV Ab II assay (Innogenetics) (left), and on the NS4-LIA test. For the NS4-LIA test, NS4-1, NS4-5, and NS4-7 peptides were synthesized based on the type 1 (HCV-1), type 2 (HC-J6) and type 3 (BR36) prototype isolate sequences as shown in Table 4, and applied as parallel lines onto a membrane strip as indicated. 1, serum BR33, 2, serum HD10, 3, serum DKH.

Figure 9

Nucleotide sequences of Core/E1 clones obtained from the PCR fragments PC-2, PC-3, and PC-4, obtained from serum BE95 (PC-2-1 (SEQ ID NO 41), PC-2-6 (SEQ ID NO 43), PC-4-1 (SEQ ID NO 45), PC-4-6 (SEQ ID NO 47), PC-3-4 (SEQ ID NO 49), and PC-3-8 (SEQ ID NO 51)) of subtype 5a isolate BE95.

A consensus sequence is shown for the Core and E1 region of isolate BE95, presented as PC C/E1 with SEQ ID NO 53. Y, C or T, R, A or G, S, C or G.

Figure 10

Alignment of nucleotide sequences of clones with SEQ ID NO 197 and 199 (PC sequences, see also SEQ ID NO 55, 57, 59) and SEQ ID NO 35, 37 and 39 (BR36 sequences) from the NS3/4 region between nucleotides 3856 to 5292, with known sequences from the corresponding region of isolates HCV-1, HCV-J, HC-J6, and HC-J8.

Figure 11

Alignment of amino acid sequences of subtype 5a BE95 isolate PC clones with SEQ ID NO 56 and 58, from the NS3/4 region between amino acids 1286 to 1764, with known sequences from the corresponding region of isolates HCV-1, HCV-J, HC-J6, and HC-J8.

Figure 12

Alignment of amino acid sequences of subtype 5a isolate BE95 (SEQ ID NO 158) in the E1/E2 region spanning positions 328 to 546, with known sequences from the corresponding region of isolates HCV-1, HCV-J, HC-J6, HC-J8, NZL1 and HCV-TR (see Table 3).

Figure 13

Alignment of the nucleotide sequences of subtype 5a isolate BE95 (SEQ ID NO 157) in the E1/E2 region with known HCV sequences as shown in Table 3.

EXAMPLES

Example 1: The NS5b region of HCV type 3

Type 3 sera, selected by means of the INNO-LiPA HCV research kit (Stuyver et al., 1993) from a number of Brazilian blood donors, were positive in the HCV antibody ELISA (Innotest HCV Ab II; Innogenetics) and/or in the INNO-LIA HCV Ab II confirmation test (Innogenetics). Only those sera that were positive after the first round of PCR reactions (Stuyver et al., 1993) were retained for further study.

Reverse transcription and nested PCR: RNA was extracted from 50 μ l serum and subjected to cDNA synthesis as described (Stuyver et al., 1993). This cDNA was used as template for PCR, for which the total volume was increased to 50 μ l containing 10 pmoles of each primer, 3 μ l of 10x Pfu buffer 2 (Stratagene) and 2.5 U of Pfu DNA polymerase (Stratagene). The cDNA was amplified over 45 cycles consisting of 1 min 94 °C, 1 min 50 °C and 2 min 72 °C. The amplified products were separated by electrophoresis, isolated, cloned and sequenced as described (Stuyver et al., 1993).

Type 3a and 3b-specific primers in the NS5 region were selected from the published sequences (Mori et al., 1992) as follows:

for type 3a:

HCPr161(+): 5'-ACCGGAGGCCAGGAGAGTGATCTCCTCC-3' (SEQ ID NO 63) and HCPr162(-): 5'-GGGCTGCTCTATCCTCATCGACGCCATC-3' (SEQ ID NO 64);

for type 3b:

HCPr163(+): 5'-GCCAGAGGCTCGGAAGGCGATCAGCGCT-3' (SEQ ID O 65) and HCPr164(-): 5'-GAGCTGCTCTGTCCTCCTCGACGCCGCA-3' (SEQ ID NO 66)

Using the Line Probe Assay (LiPA) (Stuyver et al., 1993), seven high-titer type 3 sera were selected and subsequently analyzed with the primer sets HCPr161/162 for type 3a, and HCPr163/164 for type 3b. None of these sera was positive with the type 3b primers. NS5 PCR fragments obtained using the type 3a primers from serum BR36 (BR36-23), serum BR33 (BR33-2) and serum BR34 (BR34-4) were selected for cloning. The following sequences were obtained from the PCR fragments:

From fragment BR34-4:

BR34-4-20 (SEQ ID NO 1), BR34-4-19 (SEQ ID NO 3)

From fragment BR36-23:

BR36-23-18 (SEQ ID NO 5), BR36-23-20 (SEQ ID NO 7)

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From fragment BR33-2:

BR33-2-17 (SEQ ID NO 9), BR33-2-21 (SEQ ID NO 11)

An alignment of sequences with SEQ ID NO 1, 5 and 9 with known sequences is given in Figure 1. An alignment of the deduced amino acid sequences is shown in Figure 2. The 3 isolates are very closely related to each other (mutual homologies of about 95%) and to the published sequences of type 3a (Mori et al., 1992), but are only distantly related to type 1 and type 2 sequences (Table 5). Therefore, it is clearly demonstrated that NS5 sequences from LiPA-selected type 3 sera are indeed derived from a type 3 genome. Moreover, by analyzing the NS5 region of serum BR34, for which no 5 UR sequences were determined as described in Stuyver et al. (1993), the excellent correlation between typing by means of the LiPA and genotyping as deduced from nucleotide sequencing was further proven.

Example 2: The Core/E1 region of HCV type 3

After aligning the sequences of HCV-1 (Choo et al., 1991), HCV-J (Kato et al., 1990), HC-J6 (Okamoto et al., 1991), and HC-J8 (Okamoto et al., 1992), PCR primers were chosen regions of little sequence variation. HCP:23(+):Primers CTCATGGGGTACATTCCGCT-3' (SEQ ID NO 67) and HCPr54(-): TATTACCAGTTCATCATATCCCA-3' (SEQ ID NO 68), were synthesized on a 392 DNA/RNA synthesizer (Applied Biosystems). This set of primers was selected to amplify the sequence from nucleotide 397 to 957 encoding amino acids 140 to 319 (Kato et al., 1990): 52 amino acids from the carboxyterminus of core and 128 amino acids of El (Kato et al., 1990). The amplification products BR36-9, BRR33-1, and HD10-2 were cloned as described (Stuyver et al., 1993). The following clones were obtained from the PCR fragments:

From fragment HD10-2:

HD10-2-5 (SEQ ID NO 13), HD10-2-14 (SEQ ID NO 15), HD10-2-21 (SEQ ID NO 17) From fragment BR36-9:

BR36-9-13 (SEQ ID NO 19), BR36-9-20 (SEQ ID NO 21),

From fragment BR33-1:

BR33-1-10 (SEQ ID NO 23), BR33-1-19 (SEQ ID NO 25), BR33-1-20 (SEQ ID NO 27). An alignment of the type 3 E1 nucleotide sequences (HD10, BR36, BR33) with SEQ ID

NO 13, 19 and 23 with known E1 sequences is presented in Figure 4. Four variations were detected in the E1 clones from serum HD10 and BR36, while only 2 were found in BR33. All are silent third letter variations, with the exception of mutations at position 40 (L to P)

and 125 (M to I). The homologies of the type 3 E1 region (without core) with type 1 and 2 prototype sequences are depicted in Table 5.

In total, 8 clones covering the core/E1 region of 3 different isolates were sequenced and the E1 portion was compared with the known genotypes (Table 3) as shown in Figure 5. After computer analysis of the deduced amino acid sequence, a signal-anchor sequence at the core carboxyterminus was detected which might, through analogy with type 1b (Hijikata et al., 1991), promote cleavage before the LEWRN sequence (position 192, Fig. 5). The L-to-P mutation in one of the HD10-2 clones resides in this signal-anchor region and potentially impairs recognition by signal peptidase (computer prediction). Since no examples of such substitutions were found at this position in previously described sequences, this mutation might have resulted from reverse transcriptase or Pfu polymerase misincorporation. The 4 amino-terminal potential N-linked glycosylation sites, which are also present in HCV types la and 2, remain conserved in type 3. The N-glycosylation site in type 1b (aa 250, Kato et al., 1990) remains a unique feature of this subtype. All El cysteines, and the putative transmembrane region (aa 264 to 293, computer prediction) containing the aspartic acid at position 279, are conserved in all three HCV types. The following hypervariable regions can be delineated: V1 from aa 192 to 203 (numbering according to Kato et al., 1990). V2 (213-223), V3 (230-242), V4 (248-257), and V5 (294-303). Such hydrophilic regions are thought to be exposed to the host defense mechanisms. This variability might therefore have been induced by the host's immune response. Additional putative N-linked glycosylation sites in the V4 region in all type 1b isolates known today and in the V5 region of HC-J8 (type 2b) possibly further contribute to modulation of the immune response. Therefore, analysis of this region, in the present invention, for type 3 and 4 sequences has been instrumental in the delineation of epitopes that reside in the V-regions of E1, which will be critical for future vaccine and diagnostics development.

Example 3: The NS3/NS4 region of HCV Type 3

For the NS3/NS4 border region, the following sets of primers were selected in the regions of little sequence variability after aligning the sequences of HCV-1 (Choo et al., 1991), HCV-J (Kato et al., 1990), HC-J6 (Okamoto et al., 1991), and HC-J8 (Okamoto et al., 1992) (smaller case lettering is used for nucleotides added for cloning purposes):

set A:

HCPr116(+): 5'-ttttAAATACATCATGRCITGYATG-3' (SEQ ID NO 69)

- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70) set B:
- HCPrl16(+): 5'-ttttAAATACATCATGRCITGYATG-3' (SEQ ID NO 69)
- HCPr118(-): 5'-actagtogactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQ ID NO 71) set C:
- HCPr117(+): 5'-ttttAAATACATCGCIRCITGCATGCA-3' (SEQ ID NO 72)
- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70) set D:
- HCPr117(+): 5'-ttttAAATACATCGCIRCITGCATGCA-3' (SEQ ID NO 72)
- HCPt118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQ ID NO 71) set E:
- HCPr116(+): 5'-ttttAAATACATCATGRCITGYATG-3' (SEQ ID NO 69)
- HCPr119(-): actagtcgactaRTTIGCIATIAGCCG/TRTTCATCCAYTG-3' (SEQ ID NO 73) set F:
- HCPr117(+): 5'-mmAAATACATCGCIRCITGCATGCA-3' (SEQ ID NO 72)
- HCPr119(-): actagicgactaRTTIGCIATIAGCCG/TRTTCATCCAYTG-3' (SEQ ID NO 73) set G:
- HCPr131(+): 5'-ggaattctagaCCITCITGGGAYGARAYITGGAARTG-3' (SEQ ID NO 74)
- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70) set H:
- HCPr130(+): 5'-ggaattctagACIGCITAYCARGCIACIGTITGYGC-3' (SEQ ID NO 75)
- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70) set I:
- HCPr134(+): 5'-CATATAGATGCCCACTTCCTATC-3' (SEQ ID NO 76)
- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70) set J:
- HCPr131(+): 5'-ggaattctagaCCITCITGGGAYGARAYITGGAARTG-3' (SEQ ID NO 74)
- HCPr118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQ ID NO 71)

set K:

- HCPr130(+): 5'-ggaattctagACIGCITAYCARGCIACIGTITGYGC-3' (SEQ ID NO 75)
- HCPr118(-): 5'-actagtegactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQ ID NO 71)

set L:

HCPr134(+): 5'-CATATAGATGCCCACTTCCTATC-3' (SEQ ID NO 76)

HCPr118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQID NO 71) set M:

HCPr3(+): 5'-GTGTGCCAGGACCATC-3' (SEQ ID NO 77) and

HCPr4(-): 5'-GACATGCATGTCATGATGTA-3 (SEQ ID NO 78)

set N:

HCPr3(+): 5'-GTGTGCCAGGACCATC-3' (SEQ ID NO 77) and

HCPr118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQ ID NO 71) set O:

HCPr3(+): 5'-GTGTGCCAGGACCATC-3' (SEQ ID NO 77) and

HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70)

No PCR products could be obtained with the sets of primers A, B, C, D, E, F, G, H, I, J, K, L, M, and N, on random-primed cDNA obtained from type 3 sera. With the primer set O, no fragment could be amplified from type 3 sera. However, a smear containing a few

weakly stainable bands was obtained from serum BR36. After sequence analysis of several DNA fragments, purified and cloned from the area around 300 bp on the agarose gel, only one clone, HCCl53 (SEQ ID NO 29), was shown to contain HCV information. This

A new primer set P was subsequently tested on several sera.

set P:

HCPr152(+): 5'-TACGCCTCTTCTATATCGGTTGGGGCCTG-3' (SEQ ID NO 79) and

HCPr66(-): 5'-CTATTATTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70)

The 464-bp HCPr152/66 fragment was obtained from serum BR36 (BR36-20) and serum HD10 (HD10-1). The following clones were obtained from these PCR products:

From fragment HD10-1:

sequence was used to design primer HCPr152.

HD10-1-25 (SEQ ID NO 31), HD10-1-3 (SEQ ID NO 33),

From fragment BR36-20:

BR36-20-164 (SEQ ID NO 35), BR36-20-165 (SEQ ID NO 37), BR36-20-166 (SEQ ID NO 39),

The nucleotide sequences obtained from clones with SEQ ID NO 29, 31, 33, 35, 37 or 39 are shown aligned with the sequences of prototype isolates of other types of HCV in Figure 6. In addition to one silent 3rd letter variation, one 2nd letter mutation resulted in an

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E to G substitution at position 175 of the deduced amino acid sequence of BR36 (Fig. 7). Serum HD10 clones were completely identical. The two type 3 isolates were nearly 94% homologous in this NS4 region. The homologies with other types are presented in Table 5.

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Example 4: Analysis of the anti-NS4 response to type-specific peptides

As the NS4 sequence contains the information for an important epitope cluster, and since antibodies towards this region seem to exhibit little cross-reactivity (Chan et al., 1991), it was worthwhile to investigate the type-specific antibody response to this region. For each of the 3 genotypes, HCV-1 (Choo et al., 1991), HC-J6 (Okamoto et al., 1991) and BR36 (present invention), three 20-mer peptides were synthesized covering the epitope region between amino acids 1688 and 1743 (as depicted in table 6). The synthetic peptides were applied as parallel lines onto membrane strips. Detection of anti-NS4 antibodies and color development was performed according to the procedure described for the INNO-LIA HCV Ab II kit (Innogenetics, Antwerp). Peptide synthesis was carried out on a 9050 PepSynthesizer (Millipore). After incubation with 15 LiPA-selected type 3 sera, 9 samples showed reactivity towards NS4 peptides of at least 2 different types, but a clearly positive reaction was observed for 3 sera (serum BR33, HD30 and DKH) on the type 3 peptides, while negative (serum BR33 and HD30) or indeterminate (serum DKH) on the type 1 and type 2 NS4 peptides; 3 sera tested negative for anti-NS4 antibodies (Figure 8). Using the same membrane strips coated with the 9 peptides as indicated above and as shown in Figure 8. 38 type 1 sera (10 type 1a and 28 type 1b), 11 type 2 sera (10 type 2a and 1 type 2b), 12 type 3a sera and 2 type 4 sera (as determined by the LiPA procedure) were also tested. As shown in Table 8, the sera reacted in a genotype-specific manner with the NS4 epitopes. These results demonstrate that type-specific anti-NS4 antibodies can be detected in the sera of some patients. Such genotype-specific synthetic peptides might be employed to develop serotyping assays, for example a mixture of the nine peptides as indicated above, or combined with the NS4 peptides from the HCV type 4 or 6 genotype or from new genotypes corresponding to the region between amino acids 1688 and 1743, or synthetic peptides of the NS4 region between amino acids 1688 and 1743 of at least one of the 6 genotypes, combined with the E1 protein or deletion mutants thereof, or synthetic E1 peptides of at least one of the genotypes. Such compositions could be further extended with type-specific peptides or proteins, including for example the region between amino acids 68 and 91 of the core protein, or more preferably the region between amino acids 68 and 78. Furthermore, such type-specific antigens may be advantageously used to improve current diagnostic screening and confirmation assays and/or HCV vaccines.

Example 5 The Core and E1 regions of HCV type 5

Sample BE95 was selected from a group of sera that reacted positive in a prototype Line Probe Assay as described earlier (Stuyver et al., 1993), because a high-titer of HCV RNA could be detected, enabling cloning of fragments by a single round of PCR. As no sequences from any coding region of type 5 has been disclosed yet, synthetic oligonucleotides for PCR amplification were chosen in the regions of little sequence variation after aligning the sequences of HCV-1 (Choo et al., 1991), HCV-J (Kato et al., 1990), HC-J6 (Okamoto et al., 1991), HC-J8 (Okamoto et al., 1992), and the new type 3 sequences of the present invention HD10, BR33, and BR36 (see Figure 5, Example 2). The following sets of primers were synthesized on a 392 DNA/RNA-synthesizer (Applied Biosystems):

Set 1:

HCPr52(+): 5'-atgTTGGGTAAGGTCATCGATACCCT-3' (SEQ ID NO 80) and

HCPr54(-): 5'-ctattaCCAGTTCATCATCATATCCCA-3' (SEQ ID NO 78)

Set 2:

HCPr41(+): 5'-CCCGGGAGGTCTCGTAGACCGTGCA-3' (SEQ ID NO 81) and

HCPr40(-): 5'-ctattaAAGATAGAGAAAGAGCAACCGGG-3'(SEQ ID NO 82)

Set 3:

HCPr41(+): 5'-CCCGGGAGGTCTCGTAGACCGTGCA-3' (SEQ ID NO 81) and

HCPr54(-): 5'-ccattaCCAGTTCATCATCATATCCCA-3' (SEQ ID NO 78)

The three sets of primers were employed to amplify the regions of the type 5 isolate PC as described (Stuyver et al., 1993). Set 1 was used to amplify the E1 region and yielded fragment PC-4, set 2 was designed to yield the Core region and yielded fragment PC-2. Set 3 was used to amplify the Core and E1 region and yielded fragment PC-3. These fragments were cloned as described (Stuyver et al., 1993). The following clones were obtained from the PCR fragments:

From fragment PC-2:

PC-2-1 (SEQ ID NO 41), PC-2-6 (SEQ ID NO 43),

From fragment PC-4:

PC-4-1 (SEQ ID NO 45), PC-4-6 (SEQ ID NO 47),

From fragment PC-3:

PC-3-4 (SEQ ID NO 49), PC-3-8 (SEQ ID NO 51)

An alignment of sequences with SEQ ID NO 41, 43, 45, 47, 49 and 51, is given in Figure 9. A consensus amino acid sequence (PC C/E1; SEQ ID NO 54) can be deduced from each of the 2 clones cloned from each of the three PCR fragments as depicted in Figure 5, which overlaps the region between nucleotides 1 and 957 (Kato et al., 1990). The 6 clones are very closely related to each other (mutual homologies of about 99.7%).

An alignment of nucleotide sequence with SEQ ID NO 53 or 151 (PC C/E1 from isolate BE95) with known nucleotide sequences from the Core/E1 region is given in Figure 3. The clone is only distantly related to type 1, type 2, type 3 and type 4 sequences (Table 5).

Example 6: NS3/NS4 region of HCV type 5

Attempts were undertaken to clone the NS3/NS4 region of the isolate BE95, described in example 5. The following sets of primers were selected in the regions of little sequence variability after aligning the sequences of HCV-1 (Choo et al., 1991), HCV-J (Kato et al., 1991), HC-J6 (Okamoto et al., 1991), and HC-J8 (Okamoto et al., 1992) and of the sequences obtained from type 3 sera of the present invention (SEQ ID NO 31, 33, 35, 37 and 39); smaller case lettering is used for nucleotides added for cloning purposes:

set A:

HCP7116(+): 5'-ttttAAATACATCATGRCITGYATG-3' (SEQ ID NO 66)

HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70) set B:

HCPr116(+): 5'-ttttAAATACATCATGRCITGYATG-3' (SEQ ID NO 69)

HCPr118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQ ID NO 71) set C:

HCPr117(+): 5'-ttttAAATACATCGCIRCITGCATGCA-3' (SEQ ID NO 72)

HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70) set D:

HCPr117(+): 5'-ttttAAATACATCGCIRCITGCATGCA-3' (SEQ ID NO 72)

HCPr118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQ ID NO 71) set E:

HCPr116(+): 5'-ttttAAATACATCATGRCITGYATG-3' (SEQ ID NO 69)

HCPr119(-): actagtcgactaRTTIGCIATIAGCCG/TRTTCATCCAYTG-3' (SEQ ID NO 73)

set F:

- HCPr117(+): 5'-ttttAAATACATCGCIRCITGCATGCA-3' (SEQ ID NO 72)
- HCPr119(-): actagtcgactaRTTIGCIATIAGCCG/TRTTCATCCAYTG-3' (SEQ ID NO 73) set G:
- HCPr131(+): 5'-ggaattctagaCCITCITGGGAYGARAYITGGAARTG-3' (SEQ ID NO 74)
- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70) set H:
- HCPr130(+): 5'-ggaattctagACIGCITAYCARGCIACIGTITGYGC-3' (SEQ ID NO 75)
- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70) set I:
- HCPr134(+): 5'-CATATAGATGCCCACTTCCTATC-3' (SEQ ID NO 76)
- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70) set J:
- HCPr131(+): 5'-ggaattctagaCCITCITGGGAYGARAYITGGAARTG-3' (SEQ ID 74)
- HCPr118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQID NO 71) set K:
- HCPr130(+): 5'-ggaattctagACIGCITAYCARGCIACIGTITGYGC-3' (SEQ ID NO 75)
- HCPr118(-): 5'-actagtcgactaYTGIATICCRCTLATRWARTTCCACAT-3' (SEQ ID NO 71) set L:
- HCPr134(+): 5'-CATATAGATGCCCACTTCCTATC-3' (SEQ ID NO 76)
- HCPr118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQ ID NO 71) set M:
- HCPr3(+): 5'-GTGTGCCAGGACCATC-3' (SEQ ID NO 77) and
- HCPr4(-): 5'-GACATGCATGTCATGATGTA-3' (SEQ ID NO 78)
 - set N:
- HCPr3(+): 5'-GTGTGCCAGGACCATC-3' (SEQ ID NO 77) and
- HCPr118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQ ID NO 71)

set O:

- HCPr3(+): 5'-GTGTGCCAGGACCATC-3' (SEQ ID NO 77) and
- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEO ID NO 70)
 - No PCR products could be obtained with the sets of primers A, B, C, D, E, F, G,
- H, I, J, K, L, M, and N, on random-primed cDNA obtained from type 3 sera. However,

set O yielded what appeared to be a PCR artifact fragment estimated about 1450 base pairs, instead of the expected 628 base pairs. Although it is not expected that PCR artifact fragments contain information of the gene or genome that was targetted in the experiment, efforts were put in cloning of this artifact fragment, which was designated fragment PC-1. The following clones, were obtained from fragment PC-1:

PC-1-37 (SEQ ID NO 59 and SEQ ID NO 55), PC-1-48 (SEQ ID NO 61 and SEQ ID NO 57)

The sequences obtained from the 5' and 3' ends of the clones are given in SEQ ID NOS 55, 57, 59, and 61, and the complete sequences with SEQ ID NO 197 and 199 are shown aligned with the sequences of prototype isolates of other types of HCV in Figure 10 and the alignment of the deduced amino acid sequences is shown in Figure 11 and 7. Surprisingly, the PCR artifact clone contained HCV information. The positions of the sequences within the HCV genome are compatible with a contiguous HCV sequence of 1437 nucleotides, which was the estimated size of the cloned PCR artifact fragment. Primer HCPr66 primed correctly at the expected position in the HCV genome. Therefore, primer HCPr3 must have incidentally misprimed at a position 809 nucleotides upstream of its legitimate position in the HCV genome. This could not be expected since no sequence information was available from a coding region of type 5.

Example 7: The E2 region of HCV type 5

Serum BE95 was chosen for experiments aimed at amplifying a part of the E2 region of HCV type 5.

After aligning the sequences of HCV-1 (2), HCV-J(1), HC-J6 (3), and HC-J8 (4), PCR primers were chosen in those regions of little sequence variation.

Primers HCPr109(+): 5'-TGGGATATGATGATGATGACTGGTC-3' (SEQ ID NO 141) and HCPr14(-): 5'-CCAGGTACAACCGAACCAATTGCC-3' (SEQ ID NO 142) were combined to amplify the aminoterminal region of the E2/NS1 region, and were synthesized on a 392 DNA/RNA synthesizer (Applied Biosystems). With primers HCPr109 and HCPr14, a PCR fragment of 661 bp was generated, containing 169 nucleodtides corresponding to the E1 carboxyterminus and 492 bases from the region encoding the E2 aminoterminus.

An alignment of the type 5 E1/E2 sequences with seq ID NO. 158 with known sequences is presented in Figure 10. The deduced protein sequence was compared with the different

genotypes (Fig. 12, amino acids 328-546). In the E1 region, there were no extra structural important motifs found. The aminoterminal part of E2 was hypervariable when compared with the other genotypes. All 6 N-glycosylation sites and all 7 cysteine residue's were conserved in this E2 region. To preserve alignment, it was necessary to introduce a gap between aa 474 and 475 as for type 3a, but not between aa 480 and 481, as for type 2.

Example 8: The NS5b region of HCV type 4

Type 4 sera GB48, GB116, GB215, and GB358, selected by means of the line probe assay (LiPA, Stuyver et al., 1993), as well as sera GB549 and GB809 that could not be typed by means of this LiPA (only hybridization was observed with the universal probes), were selected from Gabonese patients. All these sera were positive after the first round of PCR reactions for the 5' untranslated region (Stuyver et al., 1993) and were retained for further study.

RNA was isolated from the sera and cDNA synthesized as described in example 1.

Universal primers in the NS5 region were selected after alignment of the published sequences as follows:

HCPr206(+): 5'-TGGGGATCCCGTATGATACCCGCTGCTTTGA-3'

(SEQ ID NO. 124) and

HCPr207(-): 5'-GGCGGAATTCCTGGTCATAGCCTCCGTGAA-3'

(SEO ID NO. 125);

and were synthesized on a 392 DNA/RNA synthesizer (Applied Biosystems). Using the Line Probe Assay (LiPA), four high-titer type 4 sera and 2 sera that could not be classified were selected and subsequently analyzed with the primer set HCPr206/207. NS5 PCR fragments obtained using these primers from serum GB48 (GB48-3), serum GB116 (GB116-3), serum GB215 (GB215-3), serum GB358 (GB358-3), serum GB549 (GB549-3), and serum GB809 (GB809-3), were selected for cloning. The following sequences were obtained from the PCR fragments:

From fragment GB48-3: GB48-3-10 (SEQ ID NO. 106)

From fragment GB116-3: GB116-3-5 (SEQ ID NO. 108)

From fragment GB215-3: GB215-3-8 (SEQ ID NO. 110)

From fragment GB358-3: GB358-3-3 (SEQ ID NO. 112)

From fragment GB549-3: GB549-3-6 (SEQ ID NO. 114)

From fragment GB809-3: GB809-3-1 (SEQ ID NO. 116)

An alignment of nucleotide sequences with SEQ ID NO. 106, 108, 110, 112, 114, and 116 with known sequences is given in Figure 1. An alignment of deduced amino acid sequences with SEQ ID NO. 107, 109, 111, 113, 115, and 117 with known sequences is given in Figure 2. The 4 isolates that had been typed as type 4 by means of LiPA are very closely related to each other (mutual homologies of about 95%), but are only distantly related to type 1, type 2, and type 3 sequences (e.g. GB358 shows homologies of 65.6 to 67.7% with other genotypes, Table 4). The sequence obtained from sera GB549 and GB809 also show similar homologies with genotypes 1, 2, and 3 (65.9 to 68.8% for GB549 and 65.0 to 68.5% for GB809, Table 4), but an intermediate homology of 79.7 to 86.8% (often observed between subtypes of the same type) exists between GB549 or GB809 with the group of isolates consisting of GB48, GB116, GB215, and GB358, or between GB549 and GB809. These data indicate the discovery of 3 new subtypes within the HCV genotype 4: in the present invention, these 3 subtypes are designated subtype 4c, represented by isolates GB48, GB116, GB215, and GB358, subtype 4g, represented by isolate GB549, and subtype 4e, represented by isolate GB809. Although the homologies observed between subtypes in the NS5 region seem to indicate a closer relationship between subtypes 4c and 4e, the homologies observed in the E1 region indicate that subtypes 4g and 4e show the closest relation (see example 8).

Example 9: The Core/E1 region of HCV type 4

From each of the 3 new type 4 subtypes, one representative serum was selected for cloning experiments in the Core/E1 region. GB549 (subtype 4g) and GB809 (subtype 4e) were analyzed together with isolate GB358 that was chosen from the subtype 4c group.

Synthetic oligonucleotides:

After aligning the sequences of HCV-1 (2), HCV-J(1), HC-J6 (3), and HC-J8 (4), PCR primers were chosen in those regions of little sequence variation.

Primers HCPr52(+): 5'-atgTTGGGTAAGGTCATCGATACCCT-3', HCPr23(+): 5'-CTCATGGGGTAAGGTCATCGATACCCT-3', a nd HCPr54(-): 5'-CTATTACCAGTTCATCATCATATCCCA-3', were synthesized on a 392 DNA/RNA synthesizer (Applied Biosystems). The sets of primers HCPr23/54 and HCPr52/54 were used. but only with the primer set HCPr52/54, PCR fragments could be obtained. This set of primers amplified the sequence from nucleotide 379 to 957 encoding amino acids 127 to 319: 65 amino acids from the carboxyterminus of core and 128 amino acids of E1. The

amplification products GB358-4, GB549-4, and GB809-4 were cloned as described in example 1. The following clones were obtained from the PCR fragments:

From fragment GB358-4: GB358-4-1 (SEQ ID NO 118)

From fragment GB549-4: GB549-4-3 (SEQ ID NO 120)

From fragment GB809-4: GB809-4-3 (SEQ ID NO 122)

An alignment of the type 4 Core/El nucleotide sequences with seq ID NO. 118, 120, and 122 with known sequences is presented in Figure 4. The homologies of the type 4 El region (without core) with type 1, type 2, type 3, and type 5 prototype sequences are depicted in Table 4. Homologies of 53 to 66% are observed with representative isolates of non-type 4 genotypes. Observed homologies in the El region within type 4, between the different subtypes, ranges from 75.2 to 78.4%. The recently disclosed sequences of the core region of Egyptian type 4 isolates (for example EG-29 in Figure 3) described by Simmonds et al. (1993) do not allow alignment with the Gabonese sequences (as described in the present invention) in the NSB region and may belong to different type 4 subtypes(s) as can be deduced from the core sequences. The deduced amino acid sequences with SEQ ID NO 119, 121, and 123 are aligned with other prototype sequences in Figure 5. Again, type-specific variation mainly resides in the variable V regions, designated in the present invention, and therefore, type-4-specific amino acids or V regions will be instrumental in diagnosis and therapeutics for HCV type 4.

Example 10: The Core/E1 and NS5b regions of new HCV type 2, 3 and 4 subtypes

Samples NE92 (subtype 2d), BE98 (subtype 3c), CAM600 and GB809 (subtype 4e), CAMG22 and CAMG27 (subtype 4f), GB438 (subtype 4h), CAR4/1205 subtype (4i), CAR1/501 (subtype 4j), CAR1/901 (subtype 4?), and GB724 (subtype 4?) were selected from a group of sera that reacted positive but aberrantly in a prototype Line Probe Assay as described earlier (Stuyver et al., 1993). Another type 5a isolate BE100 was also analyzed in the C/E1 region, and yet another type 5a isolate BE96 in the NS5b region. A high-titer of HCV RNA could be detected, enabling cloning of fragments by a single round of PCR. As no sequences from any coding region of these subtypes had been disclosed yet, synthetic oligonucleotides for PCR amplification were chosen in the regions of little sequence variation after aligning the sequences of HCV-1 (Choo et al., 1991), HCV-J(Kato et al., 1990), HC-J6 (Okamoto et al., 1991), HC-J8 (Okamoto et al., 1992), and the other new sequences of the present invention.

The above mentioned sets 1, 2 and 3 (see example 5) of primers were used, but only with set 1, PCR fragments could be obtained from all isolates (except for BE98, GB724, and CAR1/501). This set of primers amplified the sequence from nucleotide 379 to 957 encoding amino acids 127 to 319: 65 amino acids from the carboxyterminus of core and 128 amino acids of E1. With set 3, the core/E1 region from isolate NE92 and BE98 could be amplified, and with set 2, the core region of GB358. GB724, GB809, and CAM600 could be amplified. The amplification products were cloned as described in example 1. The following clones were obtained from the PCR fragments:

From isolate GB724, the clone with SEQ ID NO 193 from the core region.

From isolate NE92, the clone with SEQ ID NO 143

From isolate BE98, the clone from the core/E1 region of which part of the sequence has been analyzed and is given in SEQ ID NO 147,

From isolate CAM600, the clone with SEQ ID NO 167 from the E1 region, or SEQ ID NO 165 from the Core/E1 region as shown in Figure 3,

From isolate CAMG22, the clone with SEQ ID NO 171 from the E1 region as shown in Figure 4.

from isolate GB358, the clone with SEQ ID NO 191 in the core region,.

from isolate CAMG27, the clone with SEQ ID NO 173 from the core/E1 region,

from isolate GB438, the clone with SEQ ID NO 177 from the core/ E1 region.

from isolate CAR4/1205, the clone with SEQ ID NO 179 from the core/E1 region,

from isolate CAR1/901, the clone with SEQ ID NO 181 from the core/ E1 region,

from isolate GB809, the clone GB809-4 with SEQ ID NO 189 from the core/E1 region,

clone GB809-2 with SEQ ID NO 169 from the core/E1 region and the clone with SEQ ID NO 163 from the core region,

and from isolate BE100, the clone with SEQ ID NO 155 from the Core/E1 region as shown in Figure 4.

An alignment of these Core/E1 sequences with known Core/E1 sequences is presented in Figure 4. The deduced amino acid sequences with SEQ ID NO 144, 148, 164, 168, 170, 172, 174, 178, 180, 182, 190, 192, 194, 156, 166 are aligned with other prototype sequences in Figure 5. Again, type-specific variation mainly resides in the variable V regions, designated in the present invention, and therefore, type 2d, 3c and type 4-specific amino acids or V regions will be instrumental in diagnosis and therapeutics for HCV type (subtype) 2d, 3c or the different type 4 subtypes.

The NS5b region of isolates NE92, BE98, CAM600, CAMG22, GB438, CAR4/1205, CAR1/501, and BE96 was amplified with primers HCPr206 and HCPr207 (Table 7). The corresponding clones were cloned and sequenced as in example 1 and the corresponding sequences (of which BE98 was partly sequenced) received the following identification numbers:

NE92: SEQ ID NO 145

BE98: SEQ ID NO 149

CAM600: SEQ ID NO 201

CAMG22: SEQ ID NO 203

GB438: SEQ ID NO 207

CAR4/1205: SEQ ID NO 209

CAR1/501: SEQ ID NO 211

BE95: SEQ ID NO 159

BE96: SEQ ID NO 161

An alignment of these NS5b sequences with known NS5b sequences is presented in Figure 1. The deduced amino acid sequences with SEQ ID NO 146, 150, 202, 204, 206, 208, 210, 212, 160, 162 are aligned with other prototype sequences in Figure 2. Again, subtype-specific variations can be observed, and therefore, type 2d, 3c and type 4-specific amino acids or V regions will be instrumental in diagnosis and therapeutics for HCV type (subtype) 2d, 3c or the different type 4 subtypes.

Example 11: Genotype-specific reactivity of anti-E1 antibodies (Serotyping)

El proteins were expressed from vaccinia virus constructs containing a core/El region extending from nucleotide positions 355 to 978 (Core/El clones described in previous examples including the primers HCPr52 and HCPr54), and expressed proteins from L119 (after the initiator methionine) to W326 of the HCV polyprotein. The expressed protein was modified upon expression in the appropriate host cells (e.g. HeLa, RK13, HuTK-, HepG2) by cleavage between amino acids 191 and 192 of the HCV polyprotein and by the addition of high-mannose type carbohydrate motifs. Therefore, a 30 to 32 kDa glycoprotein could be observed on western blot by means of detection with serum from patients with hepatitis C.

As a reference, a genotype 1b clone obtained form the isolate HCV-B was also expressed in an identical way as described above, and was expressed from recombinant vaccinia virus vvHCV-11A.

A panel of 104 genotyped sera was first tested for reactivity with a cell lysate containing type 1b protein expressed from the recombinant vaccinia virus vvHCV-11A, and compared with cell lysate of RK13 cells infected with a wild type vaccinia virus ('E1/WT'). The lysates were coated as a 1/20 dilution on a normal ELISA microtiter plate (Nunc maxisorb) and left to react with a 1/20 dilution of the respective sera. The panel consisted of 14 type 1a, 38 type 1b, 21 type 2, 21 type 3a, and 9 type 4 sera. Human antibodies were subsequently detected by a goat anti-human IgG conjugated with peroxidase and the enzyme activity was detected. The optical density values of the E1 and wild type lysates were divided and a factor 2 was taken as the cut-off. The results are given in the table A. Eleven out of 14 type 1a sera (79%), 25 out of 38 type 1b sera (66%), 6 out of 21 (29%), 5 out of 21 (24%), and none of the 9 type 4 or the type 5 serum reacted (0%). These experiments clearly show the high prevalence of anti-E1 antibodies reactive with the type 1 E1 protein in patients infected with type 1 (36/52 (69%)) (either type 1a or type 1b), but the low prevalence or absence in non-type 1 sera (11/52 (21%)).

TABLE A

serum	E1/WT	,
type 1a		
3748	3.15	
3807	3.51	
5282	1.99	
9321	3.12	
9324	2.76	
9325	6.12	1
9326	10.56	
9356	1.79	
9388	3.5	
8366	10.72	
8380	2.27	
10925	4.02	
10936	2.01	
10938	1.36	

		_
type 1b		
5205 5205 5222 5246 5250 5493 5573 8243 8244 8316 8358 9337 9410 9413 10905 10919 10928 10929 10931 10932 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60	2.25 1.33 1.24 13.58 0.87 1.75 1.77 2.05 1.21 5.04 14.47 5 5.51 1.26 5.00 8.72 8.26 2.3 4.41 2.37 3.14 4.37 5.68 2.97 1.18 9.85 4.51 1.11 5.20 0.98 1.48 1.06 3.85 7.6	
61 62	7.82 1.92	

type 2	
23	0.91
24	1.16
25	2.51
26	0.96
27	1.20
28	0.96
29	2.58
30	8.05
31	0.92
32	0.82
33	5.75
34	0.79
35	0.86
36	0.85
37	0.76
38	0.92
39	1.08
40	2.33
41	2.83
42	1.21
43	0.91
type 3 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	6.88 1.47 3.06 6.52 10.24 2.72 1.11 1.54 1.60 1.21 1.07 1.00 0.85 0.96 0.51 1.00 1.09
18	0.99
19	1.04
20	1.04
21	0.96

type 4	
22	0.87
G B 48	0.49
GB113	0.68
GB116	0.73
GB215	0.52
GB358	0.56
GB359	0.71
GB438	1.08
G B 516	1.04
type 5	
BE95	0.86

Core/E1 clones of isolates BR36 (type 3a) and BE95 (type 5a) were subsequently recombined into the viruses vvHCV-62 and vvHCV-63, respectively. A genotyped panel of sera was subsequently tested onto cell lysates obtained from RK13 cells infected with the recombinant viruses vvHCV-62 and vvHCV-63. Tests were carried out as described above and the results are given in the table given below (TABLE B). From these results, it can clearly be seen that, although some cross-reactivity occurs (especially between type 1 and 3), the obtained values of a given serum are usually higher on its homologous El protein than on an El protein of another genotype. For type 5 sera, none of the 5 sera were reactive on type 1 or 3 Ei proteins, while 3 out of 5 were shown to contain anti-E1 antibodies when tested on their homologous type 5 protein. Therefore, in this simple test system, a considerable number of sera can already be serotyped. Combined with the reactivity to type-specific NS4 epitopes or epitopes derived from other type-specific parts of the HCV polyprotein, a serotyping assay may be developed for discriminating the major types of HCV. To overcome the problem of cross-reactivity, the position of cross-reactive epitopes may be determined by someone skilled in the art (e.g. by means of competition of the reactivity with synthetic peptides), and the epitopes evoking cross-reactivity may be left out of the composition to be included in the serotyping assay or may be included in sample diluent to outcompete cross-reactive antibodies.

TABLE B

serum	E1 ^{1b} /WT	E13a/WT	E1 ⁵ */WT	
type 1b				
8316 8358 9337 9410 9413 10905 10919 10928 10929 10931 5 6 7 8 9 10 11 12 13 14	0.89 2.22 1.59 16.32 9.89 1.04 3.17 4.39 2.95 3.11 0.86 3.48 6.76 10.88 1.76 9.88 8.48 0.76 5.04 10.48 5.18	0.59 2.65 0.96 9.60 2.91 0.96 2.56 2.28 2.07 1.49 0.86 1.32 4.00 3.44 1.88 7.48 8.99 0.72 5.67 10.54 1.62	0.80 1.96 0.93 3.62 2.85 1.05 2.96 2.07 2.08 2.11 0.96 1.32 3.77 4.04 1.58 7.20 8.45 0.76 5.37 11.22 1.65	
type 3				
8332 10907 10908 10934 10927 8210 8344 8351 30	3.39 3.24 0.99 0.86 2.58 0.82 1.09 1.21 0.85 0.85	4.22 4.39 0.94 0.90 2.71 0.80 6.66 1.29 4.11 2.16	0.66 0.96 0.98 0.90 2.44 0.86 1.17 1.22 0.98 1.04	
type 5	0.78	0.05		
BE110 BE95 BE111 BE112 BE113	0.78 0.79 0.47 0.71 1.01	0.95 1.01 0.52 0.75 1.27 1.35	1.54 4.95 0.65 8.33 2.37 1.60	

Table 5. Homologies of new HCV sequences with other known HCV types

Region (nucleotides)	Isolate (type)	la HCV-1	lb HCV-J	2a HC-J6	2b HC-J8	Τl	3a T7	3 T9	ь Т10
Core (1-573)	PC (5)	83 8 (91.6)	84.3 (92.1)	82.6 (90])	82.4 (89.0)				
E1 (574-957)	HD10 (3) BR36 (3) BR33 (3) PC (5) GB358 (4a) GB549 (4b) GB809 (4c)	66 0 (72.2)	64 6 (68.8) 62.5 (67.2) 63.3 (68.0) 62.4 (64.8) 62.3 (65.9) 62.8 (69.8) 60.7 (64.3)	`	56.3 (59.4) 55.2 (58.6) 56.0 (58.6) 53.3 (47.2) 54.4 (54.0) 56.5 (54.0) 53.0 (51.6)				
NS3 (3856-4209)	PC (5)	74 7 (89)	76.1 (86 4)	76.1 (89 8)	78 0 (89 0)				
NS4 (4892-5292)	BR36 (3) HD 10 (3)	67 8 (78.5) 69 8 (74.6)	, ,	1	61 7 (66 0) 59 1 (59 9)				
NS4 (4936-5292)	PC (5)	61 3 (62 2)	63 0 (65 5)	52 9 (46 2)	54 3 (43 7)				
NS5b (8023-8235)	BR34 (3) BR36 (3) BR33 (3) GB358 (4a) GB549 (4b) GB809 (4c)	68 8 (76.1)	67.1 (77 0)	1	65 9 (74 4)		93 4	75 6 75 1 76 0	77.0 76 5 77 5

Shown are the nucleotide homologies (the amino-acid homology is given between brackets) for the region indicated in the left column

Table 6. NS4 sequences of the different genotypes

prototype	TYPE	SYNTHETIC PEPTIDE NS4-1 (NS44)	SYNTHETIC PEPTIDE NS±5 (NS48)	SYNTHETIC PEPTIDE NS (NS46)		
position->		1 1 6 7 9 0 0 0	1 1 7 - 2 3 0 0	1 1 7 7 3 4 0 0		
HCV-I	la	LSG KPAIIPDREV LY <u>RE</u> FDE	SQHLPYTEQ GMMLAEQFKQ K	LAEOFKO RALGILOTAS ROA		
HCV-J	lb	LSG RPAVIPDREV LYQEFDE	ASHLPYIEQ GMOLAEQFKQ R	LAEQFKQ KALGLLQTAT KQA		
HC-16	2a	<u>VNO</u> R <u>AV</u> V <u>A</u> PDKEV LY <u>E</u> AFDE	ASRAALIEE GORIAEMLES K	IAE <u>MLES</u> <u>Kio</u> gllooas koa		
HC-18	26	L <u>nd</u> r <u>vv</u> v <u>a</u> pdre <u>i</u> ly <u>e</u> afde	ASKAALTEE GORMAEMLES R	MAEMLES KIQGILLQQAT RQA		
BR36	За	rēc katābdken tadā āde	SQAAPYTEQ AQVIAHQFKE ;;	IAHOFKE KILIGITÖBAL ÓÓÖ		
PC 3	5	LSG KPAIIPDRE <u>A</u> LYQQ FDE V	AASLPYMDE TRAIAGOFKE K	LAGOFKE KULO <u>FIS</u> T <u>TG</u> <u>QK</u> A		

^{*,} residues conserved in every genotype. Underlined amino acids are type-specific, amino acids in italics are unique to type 3 and 5 sequences

Table 7

SEQ ID NO	Primer NO (polarity)	Sequence from 5' to 3'
63	HCPrl61(-)	5'-ACCGGAGGCCAGGAGAGTGATCTCCTCC-3'
64	HCPr162(-)	5'-GGGCTGCTCTATCCTCATCGACGCCATC-3'
65	HCPr163(+)	5'-GCCAGAGGCTCGGAAGGCGATCAGCGCT-3'
66	HCPr164(-)	5'-GAGCTGCTCTCCTCGACGCCGCA-3'
67	HCPr23(÷)	5'-CTCATGGGGTACATTCCGCT-3'
68	HCPr54(-)	5'-CTATTACCAGTTCATCATCATATCCCA-3'-
69	HCPrl16(-)	5'-ttttAAATACATCATGRCITGYATG-3'
70	HCPr66(-)	5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3'
71	HCPrl18(-)	5'actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3'
72	HCPr117(-)	5'-ttttAAATACATCGCIRCITGCATGCA-3'
73	HCPr119(-)	5'-actagtcgactaRTTIGCIATIAGCCKRTTCATCCAYTG-3'
74	HCPr131(÷)	5'-ggaattctagaCCITCITGGGAYGARAYITGGAARTG-3'
75	HCPr130(-)	5'-ggaattetagACIGCITAYCARGCIACIGTITGYGC-3'
76	HCPr134(+)	5'-CATATAGATGCCCACTTCCTATC-3'
77	HCPr3(+)	5"-GTGTGCCAGGACCATC-3"
78	HCPr4(-)	5'-GACATGCATGTCATGATGTA-3'
79	HCPr152(+)	5'-TACGCCTCTTCTATATCGGTTGGGGCCTG-3'
30	HCPr52(+)	5'-atgTTGGGTAAGGTCATCGATACCCT-3'
81	HCPr41(-)	5'-CCCGGGAGGTCTCGTAGACCGTGCA-3'
82	HCPr40(-)	5'-ctattaAAGATAGAGAAAGAGCAACCGGG-3'
124	HCPR206	5'-tggggatcccgtatgatacccgctgctttga-3'
125	HCPR207	5'-ggcggaattcctggtcatagcctccgtgaa-3'
141	HCPR109	5'-tgggatatgatgatgaactggtc-3'
142	HCPR14	5'-ccaggtacaaccgaaccaattgcc-3'

Table 8: NS4 SEROTYPING

	Type	ype 1 NS4		Type	Fype 2 NS4		Typ	Type 3 NS4	
serum	_	\$	7	-	5	7	_	νc	7
type Ia									
101	~	~	3	•	_		-/+	-/ +	3
102	_	-/+	7	,	•	~1	•	'	_
103		3	3	,	-/+	~	ı	-/+	3
104	3	3	٣	2	2	~	~	-/+	7
105	3	3	~	,	2	7	-/+	-/+	7
106	9	_	_	,	_	7	-/+	-/+	-/+
107	3	3	3	,	2	2	C1	,	_
801	3	3	т.	ı	-/+	7	-/-		C1
109	3	3	3	-/+	7	3	_	•	3
110	3		٣	•	-/+		1	,	۳.

SUBSTITUTE SHEET (RULE 26)

	Type	Type I NS4		Type	Type 2 NS4		Type	Type 3 NS4	
serum	-	ડ	7	-	5	7	-	S	7
type 1b									
=	-/+	-/+	•	,	ı	,	ı	•	ı
112	•	7	3	ı	,	7	,	•	۳
113	2	3	3	1	1	_	•	•	~
114	2	3	3	-	+	7	<u>-</u>	_	~
115	3	3	3	1	+	٣	•	1	3
116	3	3	3	ı	' /+	_	1	1	_
1117	3	•	•	3	+/-	-/+	-/+	•	,
81		2	3	•	-/+	7	,	- /-i-	٣
611	-/+	2	2	-/+	-/+	2	+	_	7
120	•	3	3	٠.	-/+	-/+	•		,
121	~	3	3	-/-	Cì	2	2	C1	
122	3	3	_	,	_	2	C1	_	
123	~-	3	2	ı	_	7		_	_
124	~	~	3		+/-	2	,	•	2

	Type	1 NS4		Type 2	c 2 NS4		Type 3	e 3 NS4	
serum	_	S	7		5	7	_	S	7
125	~	2	3		_	3	2	-	3
126	_	2	2		_	_		_	_
127	3	2	+/-	•	+/-		+/-	+/-	-/+
128	3	3	3	ı	+/-	_	C1	+,-	+/-
129	2	~	3	•		3	1	ı	۳.
130	•	2	_	+/-	1	1	,	'	
131	1			1	'	1	,	1	+/-
132	r	ı	1	-/+	,	-/+	-/-1	1	t
133	3	~	3	ı	_	~	1		3
134		7	2	1	,	•	,	,	,
135	~	3	3	_	÷	7	7		۳
136	ı	3	~	-/+	-/-	-/+	-/-	•	9
137	-/+	-/+	-/+	+/-	-/+	-/-1	-/-	ı	•
138	3	3	3	-/,-	2	2	-	-	3
type 2a									
139		,	ı	3	٣	-/+		ı	ı
140	-/+	•	•	3	3	۳.	3	1	ı
141	2		•	2	_	-/· -	7	,	,
142	,	,	,	,	-/+	ı	ı	1	
143	•	+/-	+/-		61		_	-/+	-/+
44		_	÷	_	3	7	_		2
145	•	-/+	+/-	3		C1	2	-/ i	· -/+
146	1	,	•	-/+	-/+	1	1	ı	t
147	•	-/+	1	<u>ش</u>	_	<i>ر</i> ب	,	ı	,
148			•	-/-	1	-	+/-	ı	r

	Type	Type 1 NS4		Type	Type 2 NS4		Type	Type 3 NS4	
serum		လ	7	-	5	7	-	5	7
type 2b									
149	•	-/+	-/+	3	3	_	2	-/+-	+/-
type 3									
150	-/+	-/ ŀ	-/+	-/+	-/-	-/+	 c	٠ ،	æ c
151	۱ .	•	,	· ·	: 1		3 6	•	1 1
152	-/+		•	ı ı			•	_	'
153	· /+	. –	. ~	ı	+/-	2	7		۳
154		. 2	3	ı	7	2	_		~
156	ı	•	1	, ,	• 7	ı	·	. ,	
157		1	1	-/+	-/-		<u>'</u>	1 C	. 6
158	2	1	1	1	- `i	7 +	، ر	۰	· ~
159	,	ı		,	-/-	<u>.</u>		. ~	<u>ص</u>
160		•		1	<u>-</u>		-/+	~	C1
161	,	'			-	-			
type 4									
								•	,
162		ı	•	ا 	1 7	,]	· \\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	•	ı
191	2		,	1	-/+-	-/+	_ / _	,	

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CLAIMS

- 1 A composition comprising or consisting of at least one polynucleic acid containing 8 or more contiguous nucleotides selected from at least one of the following HCV sequences.
- an HCV type 3 genomic sequence, more particularly in any of the following regions:
 - the region spanning positions 417 to 957 of the Core/E1 region of HCV subtype 3a,
 - the region spanning positions 4664 to 4730 of the NS3 region of HCV type 3,
 - the region spanning positions 4892 to 5292 of the NS3/4 region of HCV type 3,
 - the region spanning positions 8023 to 8235 of the NS5 region of HCV subtype 3a.
 - an HCV subtype 3c genomic sequence,
- an HCV subtype 2d genomic sequence,
- an HCV type 4 genomic sequence,
- the coding region of HCV subtype 5a,

with said nucleotide numbering being with respect to the numbering of HCV nucleic acids as shown in Table 1, and with said polynucleic acids containing at least one nucleotide difference with known HCV polynucleic acid sequences in the above-indicated regions, or the complement thereof

- 2. A composition according to claim 1, wherein said polynucleic acids correspond to a nucleotide sequence selected from any of the following HCV genomic sequences
- an HCV genomic sequence as having a homology of at least 67%, preferably more than 69%, most preferably 71% or more to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 in the region spanning positions 417 to 957 of the Core/E1 region;
- an HCV genomic sequence as having a homology of at least 65%, preferably more than 67%, most preferably 69% or more to any of the sequences as represented in SEQ ID NO 19, 21, 23, 25 or 27 in the region spanning positions 574 to 957 of the E1 region.
- an HCV genomic sequence, having a homology of at least 79%, more preferably at least 81%, most preferably more than 83% or more to any of the sequences as represented in

- SEQ ID NO 147 in the region spanning positions 1 to 378 of the Core region,
- an HCV genomic sequence having a homology of at least 74%, more preferably at least 76%, most preferably more than 78% or more to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 in the region spanning positions 417 to 957 in the Core/E1 region,
- an HCV genomic sequence having a homology of at least 74%, preferably more than 76%, most preferably 78% or more to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 in the region spanning positions 574 to 957 in the E1 region,
- an HCV genomic sequence having a homology of more than 73.5%, preferably more than 74%, most preferably 75% homology to any of the sequence as represented in SEQ ID NO 29 in the region spanning positions 4664 to 4730 of the NS3 region,
- an HCV genomic sequence having a homology of more than 70%, preferably more than 72%, most preferably more than 74% homology to any of the sequences as represented in SEQ ID NO 29, 31, 33, 35, 37 or 39 in the region spanning positions 4892 to 5292 in the NS3/NS4 region,
- an HCV genomic sequence having a homology of more than 95%, preferably 95,5%, most preferably 96% homology to any of the sequences as represented in SEQ ID NO 5, 7, 1, 3, 9 or 11 in the region spanning positions 8023 to 8235 of the NS5 region,
- an HCV genomic sequence of the BR36 subgroup of HCV type 3a having a homology of more than 96%, preferably 96 5%, most preferably 97% homology to any of the sequences as represented in SEQ ID NO 5, 7, 1, 3, 9 or 11 in the region spanning positions 8023 to 8192 of the NS5B region,
- an HCV genomic sequence having a homology of more than 79%, more preferably more than 81%, and most preferably more than 83% to the sequence as represented in SEQ ID NO 149 in the region spanning positions 7932 to 8271 in the NS5B region.
- 3. A composition according to claim 1, wherein said polynucleic acids correspond to a nucleotide sequence selected from any of the following HCV genomic sequences
- an HCV genomic sequence having a homology of more than 85%, preferably more than 86%, most preferably more than 87% homology to any of the sequences as represented in SEQ ID NO 41, 43, 45, 47, 49, 51, 53 or 151 in the region spanning positions 1 to 573 of the Core region,

- an HCV genomic sequence having a homology of more than 61%, preferably more than 63%, most preferably more than 65% homology to any of the sequences as represented in SEQ ID NO 41, 43, 45, 47, 49, 51, 53, 153 or 155 in the region spanning positions 574 to 957 of the E1 region,
- an HCV genomic sequence having a homology of more than 76.5%, preferably of more than 77%, most preferably of more than 78% homology with any of the sequences as represented in SEQ ID NO 55, 57, 197 or 199 in the region spanning positions 3856 to 4209 of the NS3 region;
- an HCV genomic sequence having a homology of more than 68%, preferably of more than 70%, most preferably of more than 72% homology with the sequence as represented in SEQ ID NO 157 in the region spanning positions 980 to 1179 of the E1/E2 region,
- an HCV genomic sequence having a homology of more than 57%, preferably more than 59%, most preferably more than 61% homology to any of the sequences as represented in SEQ ID NO 59 or 61 in the region spanning positions 4936 to 5296 of the NS4 region,
- an HCV genomic sequence having a homology of more than 93%, preferably more than 93.5%, most preferably more than 94% homology to any of the sequences as represented in SEQ ID NO 159 or 161 in the region spanning positions 7932 to 8271 of the NS5B region.
- 4 A composition according to claim 1, wherein said polynucleic acids correspond to a nucleotide sequence selected from any of the following HCV genomic sequences
- an HCV genomic sequence having a homology of more than 66%, preferably more than 68%, most preferably more than 70% homology in the E1 region spanning positions 574 to 957 to any of the sequences as represented in SEQ ID NO 118, 120 or 122 in the region spanning positions 1 to 957 of the Core E1 region,
- an HCV genomic sequence having a homology of more than 71%, preferably more than 72%, most preferably more than 74% homology to any of the sequences as represented in SEQ ID NO 118, 120 or 122 in the region spanning positions 379 to 957,
- an HCV genomic sequence having a homology of more than 85%, preferably more than 86%, most preferably more than 86 5% homology to any of the sequences as represented in SEQ ID NO 183, 185 or 187 in the region spanning positions 379 to 957 of the El region,
- an HCV genomic sequence having a homology of more than 81%, preferably more than

- 83%, most preferably more than 85% homology to the sequence as represented in SEQ ID NO 189 in the region spanning positions 379 to 957 of the E1 region,
- an HCV genomic sequence having a homology of more than 85%, preferably more than 87%, most preferably more than 89% homology to any of the sequences as represented in SEQ ID NO 167 or 169 in the region spanning positions 379 to 957 of the E1 region,
- an HCV genomic sequence having a homology of more than 79%, preferably more than 81%, most preferably more than 83% homology to any of the sequences as represented in SEQ ID NO 171 or 173 in the region spanning positions 379 to 957 of the E1 region.
- an HCV genomic sequence having a homology of more than 84%, preferably more than 86%, most preferably more than 88% homology to the sequence as represented in SEQ ID NO 175 in the region spanning positions 379 to 957 of the E1 region,
- an HCV genomic sequence having a homology of more than 83%, preferably more than 85%, most preferably more than 87% homology to the sequence as represented in SEQ ID NO 177 in the region spanning positions 379 to 957 of the Ei region,
- an HCV genomic sequence having a homology of more than 76%, preferably more than 78%, most preferably more than 80% homology to the sequence as represented in SEQ ID NO 179 in the region spanning positions 379 to 957 of the E1 region.
- an HCV genomic sequence having a homology of more than 84%, preferably more than 86%, most preferably more than 88% homology to the sequence as represented in SEQ ID NO 181 in the region spanning positions 379 to 957 of the E1 region ,
- an HCV genomic sequence having a homology of more than 73%, preferably more than 75%, most preferably more than 77% homology to any of the sequences as represented in SEQ ID NO 106, 108, 110, 112, 114, or 116 in the region spanning positions 7932 to 8271 of the NS5 region;
- an HCV genomic sequence having a homology of more than 88%, preferably more than 89%, most preferably more than 90% homology to any of the sequences as represented in SEQ ID NO 106, 108, 110, or 112 in the region spanning positions 7932 to 8271 of the NS5 region;
- an HCV genomic sequence having a homology of more than 88%, preferably more than 89%, most preferably more than 90% homology to any of the sequences as represented in SEQ ID NO 116 or 201 in the region spanning positions 7932 to 8271 of the NS5 region,
- an HCV genomic sequence having a homology of more than 87%, preferably more than

- 89%, most preferably more than 90% homology to the sequence as represented in SEQ ID NO 203 in the region spanning positions 7932 to 8271 of the NS5 region,
- an HCV genomic sequence having a homology of more than 85%, preferably more than 87%, most preferably more than 89% homology to the sequence as represented in SEQ ID NO 114 in the region spanning positions 7932 to 8271 of the NS5 region;
- an HCV genomic sequence having a homology of more than 86%, preferably more than 87%, most preferably more than 88% homology to the sequence as represented in SEQ ID NO 207 in the region spanning positions 7932 to 8271 of the NS5 region,
- an HCV genomic sequence having a homology of more than 84%, preferably more than 86%, most preferably more than 88% homology to the sequence as represented in SEQ
 ID NO 209 in the region spanning positions 7932 to 8271 of the NS5 region,
- an HCV genomic sequence having a homology of more than 81%, preferably more than 83%, most preferably more than 85% homology to the sequence as represented in SEQ ID NO 211 in the region spanning positions 7932 to 8271 of the NS5 region
- 5 A composition according to claim 1, wherein said polynucleic acids correspond to a nucleotide sequence selected from any of the following HCV genomic sequences
- an HCV genomic sequence having a homology of more than 78%, preferably more than 80%, most preferably more than 82% homology to the sequence as represented in SEQ ID NO 143 in the region spanning positions 379 to 957 of the Core/E1 region.
- an HCV genomic sequence having a homology of more than 74%, preferably more than 76%, most preferably more than 78% homology to the sequence as represented in SEQ ID NO 143 in the region spanning positions 574 to 957,
- an HCV genomic sequence having a homology of more than 87%, preferably more than 89%, most preferably more than 91% homology to the sequence as represented in SEQ ID NO 145 in the region spanning positions 7932 to 8271 of the NS5B region
- A composition according to any of claims 1 to 5, wherein said polynucleic acid is liable to act as a primer for amplifying the nucleic acid of a certain isolate belonging to the genotype from which the primer is derived
- A composition according to any of claims 1 to 5, wherein said polynucleic acid is able to act as a hybridization probe for specific detection and/or classification into types of a

nucleic acid containing said nucleotide sequence, with said oligonucleotide being possibly labelled or attached to a solid substrate

- 8 Use of a composition according to any of claims 1 to 7 for *in vitro* detecting the presence of one or more HCV genotypes, more particularly for detecting the presence of a nucleic acid of any of the HCV genotypes having a nucleotide sequence as defined in any of claims 1 to 5, present in a biological sample liable to contain them, comprising at least the following steps:
 - (i) possibly extracting sample nucleic acid,
 - (ii) possibly amplifying the nucleic acid with at least one of the primers according to claim 6 or any other HCV type 2. HCV type 3, HCV type 4, HCV type 5 or universal HCV primer,
 - (iii) hybridizing the nucleic acids of the biological sample, possibly under denatured conditions, and with said nucleic acids being possibly labelled during or after amplification, at appropriate conditions with one or more probes according to claim 7, with said probes being preferably attached to a solid substrate,
 - (iv) washing at appropriate conditions,
 - (v) detecting the hybrids formed,
 - (vi) inferring the presence of one or more HCV genotypes present from the observed hybridization pattern
- 9 A composition consisting of or comprising at least one peptide or polypeptide containing in its sequence a contiguous sequence of at least 5 amino acids of an HCV polyprotein encoded by any of the polynucleic acids according to any of claims 1 to 5.
- 10 A composition according to claim 9, wherein said contiguous sequence contains in its sequence at least one of the following amino acid residues:
- L7, Q43, M44, S60, R67, Q70, T71, A79, A87, N106, K115, A127, A190, S130, V134, G142, I144, E152, A157, V158, P165, S177 or Y177, I178, V180 or E180 or F182, R184, I186, H187, T189, A190, S191 or G191, Q192 or L192 or I192 or V192 or E192, N193 or H193 or P193, W194 or Y194, H195, A197 or I197 or V197 or T197, V202, I203 or L203, Q208, A210, V212, F214, T216, R217 or D217 or E217 or V217, H218 or N218, H219 or V219 or L219, L227 or I227, M231 or E231 or Q231, T232 or D232 or A232 or K232, Q235

or I235, A237 or T237, I242, I246, S247, S248, V249, S250 or Y250, I251 or V251 or M251 or F251, D252, T254 or V254, L255 or V255, E256 or A256, M258 or F258 or V258, A260 or Q260 or S260, A261, T264 or Y264, M265, I266 or A266, A267, G268 or T268, F271 or M271 or V271, I277, M230 or H230, I234 or A284 or L84, V274, V291, N292 or S292, R293 or I293 or Y293, Q294 or R294, L297 or I297 or Q297, A299 or K299 or Q299, N303 or T303, T308 or L308, T310 or F310 or A310 or D310 or V310, L313, G317 or Q317, L333, S351, A358, A359, A363, S364, A366, T369, L373, F376, Q386, I387, S392, I399, F402, I403, R405, D454, A461, A463, T464, K484, Q500, E501, S521, K522, H524, N528, S531, S532, V534, F536, F537, M539, I546, C1282, A1283, H1310, V1312, Q1321, P1368, V1372, V1373, K1405, Q1406, S1409, A1424, A1429, C1435, S1436, S1456, H1496, A1504, D1510, D1529, I1543, N1567, D1556, N1567, M1572, Q1579, L1581, S1583, F1585, V1595, E1606 or T1606, M1611, V1612 or L1612, P1630, C1636, P1651, T1656 or I1656, L1663, V1667, V1677, A1681, H1685, E1687, G1689, V1695, A1700, Q1704, Y1705, A1713, A1714 or \$1714, M1718, D1719, A1721 or T1721, R1722, A1723 or V1723, H1726 or G1726. E1730, V1732, F1735, I1736, S1737, R1738, T1739, G1740, Q1741, K1742, Q1743, A1744, T1745, L1746, E1747 or K1747, 11749, A1750, T1751 or A1751, V1753, N1755, K1756, A1757, P1758, A1759, H1762, T1763, Y1764, P2645, A2647, K2650, K2653 or L2653, S2664, N2673, F2680, K2681, L2686, H2692, Q2695 or L2695 or I2695, V2712, F2715, V2719 or O2719, T2722, T2724, S2725, R2726, G2729, Y2735, H2739, I2748, G2746 or 12746, 12748, P2752 or K2752, P2754 or T2754, T2757 or P2757,

with said notation being composed of a letter representing the amino acid residue by its oneletter code, and a number representing the amino acid numbering according to Kato et al., 1990 as shown in Table 1

- 11 A composition according to any of claims 9 or 10, wherein said contiguous sequence is selected from any of the following HCV amino acid sequences
- a sequence having a homology of more than 72%, preferably more than 74%, and most preferably more than 77% homology to any of the amino acid sequences as represented in SEQ ID NO 14, 16, 18, 20, 22, 24, 26 or 28 in the region spanning positions 140 to 319 in the Core/E1 region,
- a sequence having a homology of more than 70%, preferably more than 72%, and most preferably more than 75% homology to any of the amino acid sequences as represented in SEQ ID NO 14, 16, 18, 20, 22, 24, 26 or 28 in the E1 region spanning positions 192 to

319,

- a sequence having a homology of more than 86%, preferably more than 88%, and most preferably more than 90% homology to the amino acid sequences as represented in SEQ
 ID NO 148 in the region spanning positions 1 to 110 in the Core region,
- a sequence having a homology of more than 76%, preferably more than 78%, most preferably more than 80% to any of the amino acid sequences as represented in SEQ ID NO 30, 32, 34, 36, 38 or 40 in the region spanning positions 1646 to 1764 in the NS3/NS4 region,
- a sequence having a homology of more than 81.5%, preferably more than 83%, and most preferably more than 86% homology to any of the amino acid sequences as represented in SEQ ID NO 14, 16, 18, 20, 22, 24, 26 or 28 in the E1 region spanning positions 192 to 319,
- a sequence having a homology of more than 86%, preferably more than 88%, most preferably more than 90% to the amino acid sequence as represented in SEQ ID NO 150 in the region spanning positions 2645 to 2757 in the NS5B region,
- 12. A composition according to any of claims 9 or 10, wherein said contiguous sequence is selected from any of the following HCV amino acid sequences:
- a sequence having a homology of more than 80%, preferably more than 82%, most preferably more than 84% homology to any of the amino acid sequences as represented in SEQ ID NO 118, 120, and 122 in the region spanning positions 127 to 319,
- a sequence having a homology of more than 73%, preferably more than 75%. most preferably more than 78% homology in the E1 region spanning positions 192 to 319 to any of the amino acid sequences as represented in SEQ ID NO 118, 120, and 122, in the region spanning positions 127 to 319,
- a sequence having more than 85%, preferably more than 86%, most preferably more than 87% homology to any of the amino acid sequences as represented in SEQ ID NO 118, 120 or 122, in the region spanning positions 192 to 319
- 13 A composition according to any of claims 9 or 10, wherein said contiguous sequence is selected from any of the following HCV amino acid sequences
- a sequence having more than 93%, preferably more than 94%, most preferably more than 95% homology in the region spanning Core positions 1 to 191 to any of the amino acid

sequences as represented in SEQ ID NO 42, 44, 46, 48, 50, 52, 54, or 152;

- a sequence having more than 73%, preferably more than 74%, most preferably more than 76% homology in the region spanning E1 positions 192 to 319 to any of the amino acid sequences as represented in SEQ ID NO 42, 44, 46, 48, 50, 52, 54, 154 or 156;
- a sequence spanning positions 1286 to 1403 of the NS3 region, with said sequence being characterized as having more than 90%, preferably more than 91%, most preferably more than 92% homology to any of the amino acid sequences represented in SEQ ID NO 56 to 58;
- a sequence spanning positions 1646 to 1764 of the NS3/4 region, with said sequence being characterized as having more than 66%, more particularly 68%, most particularly 70% or more homology to any of the amino acid sequences as represented in SEQ ID NO 60 or 62
- 14 A composition according to any of claims 9 to 10, wherein said contiguous sequence is selected from any of the following HCV amino acid sequences
- a sequence having a more than 83%, preferably more than 85%, most preferably more than 87% homology in the region spanning Core positions 1 to 319 to the amino acid sequence as represented in SEQ ID NO 144,
- a sequence having a more than 79%, preferably more than 81%, most preferably more than 84% homology in the region spanning E1 positions 192 to 319 to the amino acid sequence as represented in SEQ ID NO 144;
- a sequence having more than 95%, more particularly 96%, most particularly 97% or more homology to the amino acid sequence as represented in SEQ ID NO 146, in the region spanning positions 2645 to 2757 of the NS5B region
- 15. A composition according to any of claims 9 to 14, wherein said sequence is selected from the following peptides:

QPTGRSWGQ (SEQ ID NO 93)

RSEGRTSWAQ (SEQ ID NO 220)

RTEGRTSWAQ (SEQ ID NO 221)

SRRQPIPRARRTEGRSWAQ (SEQ ID NO 268)

LEWRNTSGLYVL (SEQ ID NO 83)

VNYRNASGIYHI (SEQ ID NO 126)

QHYRNISGIYHV (SEQ ID NO 127)
EHYRNASGIYHI (SEQ ID NO 128)
IHYRNASGIYHI (SEQ ID NO 224)
VPYRNASGIYHV (SEQ ID NO 84)
VNYRNASGIYHI (SEQ ID NO 225)
VNYRNASGVYHI (SEQ ID NO 226)
VNYHNTSGIYHL (SEQ ID NO 227)
QHYRNASGIYHV (SEQ ID NO 228)
QHYRNVSGIYHV (SEQ ID NO 229)
IHYRNASDGYYI (SEQ ID NO 230)
LQVKNTSSSYMV (SEQ ID NO 231)
VYEADDVILHT (SEQ ID NO 85)
VYETEHHILHL (SEQ ID NO 129)
VYEADHHIMHL (SEQ ID NO 130)
VYETDHHILHL (SEQ ID NO 131)
VYEADNLILHA (SEQ ID NO 86)
VWQLRAIVLHV (SEQ ID NO 232)
VYEADYHILHL (SEQ ID NO 233)
VYETDNHILHL (SEQ ID NO 234)
VYETENHILHL (SEQ ID NO 235)
VFETVHHILHL (SEQ ID NO 236)
VFETEHHILHL (SEQ ID NO 237)
VFETDHHIMHL (SEQ ID NO 238)
VYETENHILHL (SEQ ID NO 239)
VYEADALILHA (SEQ ID NO 240)
VQDGNTSTCWTPV (SEQ ID NO 87)
VQDGNTSACWTPV (SEQ ID NO 241)
VRVGNQSRCWVAL (SEQ ID NO 132
VRTGNTSRCWVPL (SEQ ID NO 133)
VRAGNVSRCWTPV (SEQ ID NO 134)
EEKGNISRCWIPV (SEQ ID NO 242)

VKTGNQSRCWVAL (SEQ ID NO 243) VRTGNQSRCWVAL (SEQ ID NO 244) VKTGNQSRCWIAL (SEQ ID NO 245)

VKTGNVSRCWIPL (SEQ ID NO 247)

VKTGNVSRCWISL (SEQ ID NO 248)

VRKDNVSRCWVQI (SEQ ID NO 249)

VRYVGATTAS (SEQ ID NO 89)

APYIGAPLES (SEQ ID NO 135)

APYVGAPLES (SEQ ID NO 136)

AVSMDAPLES (SEQ ID NO 137)

APSLGAVTAP (SEQ ID NO 90)

APSFGAVTAP (SEQ ID NO 250)

VSQPGALTKG (SEQ ID NO 251)

VKYVGATTAS (SEQ ID NO 252)

APYIGAPVES (SEQ ID NO 253)

AQHLNAPLES (SEQ ID NO 254)

SPYVGAPLEP (SEQ ID NO 255)

SPYAGAPLEP (SEQ ID NO 256)

APYLGAPLEP (SEQ ID NO 257)

APYLGAPLES (SEQ ID NO 258)

APYVGAPLES (SEQ ID NO 259)

VPYLGAPLTS (SEQ ID NO 260)

APHLRAPLSS (SEQ ID NO 261)

APYLGAPLTS (SEQ ID NO 262)

RPRRHQTVQT (SEQ ID NO 91)

QPRRHWTTQD (SEQ ID NO 138)

RPRRHWTTQD (SEQ ID NO 139)

RPRQHATVQN (SEQ ID NO 92)

RPRQHATVQD (SEQ ID NO 263)

SPQHHKFVQD (SEQ ID NO 264)

RPRRLWTTQE (SEQ ID NO 265)

PPRIHETTQD (SEQ ID NO 266)

TISYANGSGPSDDK (SEQ ID NO 267)

16 Recombinant vector, particularly for cloning and/or expression, with said recombinant

vector comprising a vector sequence, an appropriate prokaryotic, eukaryotic or viral promoter sequence followed by the nucleotide sequences as defined in claims 1 to 5, with said recombinant vector allowing the expression of any one of the HCV type 2 and/or HCV type 3 and/or type 4 and/or type 5 derived polypeptides according to any of claims 9 to 15 in a prokaryotic, or eukaryotic host, or in living mammals when injected as naked DNA, and more particularly a recombinant vector allowing the expression of any of the following HCV type 2, HCV type 3, type 4 or type 5 polypeptides spanning the following amino acid positions

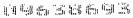
- a polypeptide starting at position 1 and ending at any position in the region between positions 70 and 326, more particularly a polypeptide spanning positions 1 to 70, 1 to 85, positions 1 to 120, positions 1 to 150, positions 1 to 191, positions 1 to 200, for expression of the Core protein, and positions 1 to 263, positions 1 to 326, for expression of the Core and E1 protein,
- a polypeptide starting at any position in the region between positions 117 and 192, and ending at any position in the region between positions 263 and 326, more particularly from positions 119 to 326, for expression of E1, or forms that have the putative membrane anchor deleted (positions 264 to 293 plus or minus 8 amino acids);
- a polypeptide starting at any position in the region between positions 1556 and 1688, and ending at any position in the region between positions 1739 and 1764, for expression of the NS4 regions, more particularly a polypeptide starting at position 1658 and ending at position 1711 for expression of the NS4a antigen, and more particularly, a polypeptide starting at position 1712 and ending between positions 1743 and 1972, for example 1712-1743, 1712-1764, 1712-1782, 1712-1972, 1712 to 1782 and 1902 to 1972 for expression of the NS4b protein or parts thereof.
- 17. A composition according to any of claims 9 to 15, wherein said polypeptide is a recombinant polypeptide expressed by means of an expression vector as defined in claim 16
- 18 A composition according to any of claims 9 to 15 or 16, for use in a method for immunizing a mammal, preferably humans, against HCV comprising administratering a sufficient amount of the composition possibly accompanied by pharmaceutically acceptable adjuvants, to produce an immune response, more particularly a vaccine composition including HCV type 3 polypeptides derived from the E1, Core, or NS4 region and/or type 4 and/or type 5 and/or type 2 polypeptides

- 19 Antibody raised upon immunization with a composition according to any of claims 9 to 15, 17 or 18, by means of a process according to claim 18, with said antibody being reactive with any of the polypeptides as defined in any of claims 9 to 15, 17 or 18
- 20 Process for detecting in vitro HCV present in biological sample liable to contain it, comprising at least the following steps:
 - (i) contacting the biological sample to be analyzed for the presence of HCV antibodies with any of the compositions according to claims 9 to 15, 17 or 18, preferentially in an immobilized form under appropriate conditions which allow the formation of an immune complex, wherein said polypeptide is preferentially in the form of a biotinylated polypeptide and is covalently bound to a solid substrate by means of streptavidin or avidin complexes,
 - (ii) removing unbound components,
 - (iii) incubating the immunecomplexes formed with heterologous antibodies, which specifically bind to the antibodies present in the sample to be analyzed, with said heterologous antibodies having conjugated to a detectable label under appropriate conditions.
 - (iv) detecting the presence of said immunecomplexes visually or by means of densitometry and inferring the HCV serotype(s) present from the observed hybridization pattern.
- 21. Use of a composition according to any of claims 9 to 15, 17 or 18, for incorporation into a serotyping assay for detecting one or more serological types of HCV present in a biological sample liable to contain it, more particularly for detecting E1 and NS4 antigens or antibodies of the different types to be detected combined in one assay format, comprising at least the following steps.
 - (i) contacting the biological sample to be analyzed for the presence of HCV antibodies or antigens of one or more serological types, with at least one of the compositions according to claims 9 to 15, 17 or 18 in an immobilized form under appropriate conditions which allow the formation of an immunecomplex, (wherein said polypeptide is preferentially in the form of a biotinylated polypeptide and is covalently bound to a solid substrate by means of streptavidin or avidin complexes),

- (ii) removing unbound components,
- (iii) incubating the immunecomplexes formed with heterologous antibodies, which specifically bind to the antibodies present in the sample to be analyzed, with said heterologous antibodies having conjugated to a detectable label under appropriate conditions.
- (iv) detecting the presence of said immunecomplexes visually or by means of densitometry and inferring the HCV serological types present from the observed binding pattern
- 22 A kit for determining the presence of HCV genotypes as defined in any of claims 1 to 5 present in a biological sample liable to contain them, comprising
 - possibly at least one primer composition containing any primer selected from those defined in claim 6 or any other HCV type 2 and/or HCV type 3 and/or HCV type 4 and/or HCV type 5, or universal HCV primers,
 - at least one probe composition according to claim 7, preferably in combination with other polypeptides or peptides from HCV type 1, type 2 or other types of HCV, with said probes being preferentially immobilized on a solid substrate, and more preferentially on one and the same membrane strip,
 - a buffer or components necessary for producing the buffer enabling hybridization reaction between these probes and the possibly amplified products to be carried out,
 - a means for detecting the hybrids resulting from the preceding hybriziation.
 - possibly also including an automated scanning and interpretation device for infering the HCV genotype(s) present in the sample from the observed hybridization pattern
- A kit for determining the presence of HCV antibodies according to any of claims 9 to 15, 17 or 18 present in a biological sample liable to contain them, comprising
 - at least one polypeptide composition according to any of claims 9 to 15, 17 or 18, with said polypeptides being preferentially immobilized on a solid substrate, and more preferentially on one and the same membrane strip,
 - a buffer or components necessary for producing the buffer enabling binding reaction between these polypeptides and the antibodies against HCV present in the biological sample,
 - a means for detecting the immune complexes formed in the preceding binding

reaction,

- possibly also including an automated scanning and interpretation device for infering the HCV genotype present in the sample from the observed binding pattern.





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(54) Title: NEW SEQUENCES OF HEPATITIS C VIRUS GENOTYPES AND THEIR USE AS THERAPEUTIC AND DIAGNOSTIC **AGENTS**

(57) Abstract

The present invention relates to a polynucleic acid composition comprising or consisting of at least one polynucleic acid containing 8 or more contiguous nucleotides corresponding to a nucleotide sequence from the region spanning positions 417 to 957 of the Core/E1 region of HCV type 3; and/or the region spanning positions 4664 to 4730 of the NS3 region of HCV type 3; and/or the region spanning positions 4892 to 5292 of the NS3/4 region of HCV type 3; and/or the region spanning positions 4892 to 5292 of the NS3/4 region of HCV type 3; and/or the region spanning positions 8 023 to 8 235 of the NS3/region of the BR36 subgroup of HCV type 3a; and/or the coding region of HCV type 4a starting at aucleotide 379 in the core region; and/or the coding region of HCV type 4; and/or the coding region of HCV type 5, with said nucleotide numbering being with respect to the numbering of HCV nucleic acids as shown in Table 1, and with said polynucleic acids containing at least one nucleotide difference with known HCV type 1, and/or HCV type 2 genomes in the above-indicated regions, or the complement thereof.

Figure 1		
		7932
HCV-1	la	ACAGTCACTGAGAGCGACATCCGTACGGAGG
HCV-J	1b	GTATA
BE90	1b	A'I''I'
2TY4	10	:
4 TY4	10	T W
HC-J6	2a	-CT'-CAAT'T'T'-G
HC-JB	2b	CGGNA-AAAAT-CAT
NE91	2b	T W
EB12	2b	- A T -
∽ ARG6	2c	1 D.T T 1 - 1 - 1
S ARG8	2c	
110	2c	- D.T T
<u>प</u> 1983	2c	
S NE92	2d	-GGGA-ATTT
南 CHR20	3а	-TACAGA-GGTA-GA
CHR21	3а	-TACAGA-GGTAAG-
CHR22	3а	-TACAGA-GGTA
Tl	3а	ACAGA-GGT'A
6 I.7	3а	-TACAGA-GG''A
NE93	3а	TACAGAGGTAG
NZL13	3а	ATACAGA-GGTAAGA
EB1	3а	∜ ¢
EB2	3а	
EB3	3а	- W -
EB7	3a	W:: 0 *
T9	3b	TACACATIA-G
T10	3b	
BE98	3с	

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		1 1 1 1	AGG-AT-	AGG-AT-	<u>,</u>	- <u>T</u> - :	-AA-A-GT-	A-GG'I'CA-AGG	A-AG	A-A(5	rcr-A-AGGT-	- <u>T</u>	ī	· T · · · · · · · · · · · · · · · · · ·	AA'j'GCAT	. {	AA'I'G'I'A'I'-'I I'	AAT'G T' A T' - C T'	
-1	7932	.CA-AG	TACA-AG	. C A - A A	.CA-AG	-GA	1	- G A A -	-GVG-	- A G	-NG	G T GN- C			- ACAT'	- C C ACAT'	T C ACAT	GCTCACAT	
Concrined		4 c	4c	4c	4c	4e	4e	4 £	49	4 h	4 i	4 j	4 k	4 K	5a	5а	5a	5a	
ridnre 1 -		GB48		GB215	35	GB809	CAM600	CAMG22	GB549		CAR4/12	= CAR1/501		EG-	BE	BE9	CH	CHR	!6)

iqure 1 - Continued 1

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	31												٠,	• •	•															
	7982	TCGACCCCCAAGCCCGCGTGGCCATCAAGTCCCTCAC	-G-CGA-GCAA-G	- G A - ACA A -	- C A T	-CACT	i i	T-AAGA-AACT-TAC-C	A-AAC'I'-'I'AC-C	-GCCT-AAG-GA-AAC'I-TAC-CG-	GTAACTAC-CA-	C-GAGG-GTAACTTAC-CA	- GCCTGAGG - G AACT T AC - C A	GCCT-AGG-GTGACTTAC-CAT-	CTT-ACC-GAGG-AGACTAC-CAG	TAGG-GA-GAAA-TG	ATAGG-GA-GAAA-TG	A'''AGG-GA-GAAA-''''	TA-GG-GA-GAGA-TG	r T G - G - G - G A - GAAA - TG T - C	TAGG-GA-GAAA-TGTCC	ATAGG-GA-GAAA-TGTCC	ATAGG-GA-GAAA-TGTCCG-	ATAGG-GA-GAAA-TGTCC	G-GA-AAAA-T'GT'C'C		֖֖֖֖֖֖֖֖֖֖֖֖֖֡֝֟֜֜֝֓֓֓֓֓֓֓֓֓֓֓֓֓֓֓֓֓֓֡֜֜֝֓֡֓֡֓֡֓֡֓֡֓֡֓֡֓	W: 'D: ': '		.C'Y'GAG-GTG/MG-G-G-1A
inued 2	SEQ ID	!		213					215						145						217						-	1,3	-	
- Conti		1a	1 p	1 p	10	10	2a	2b	2.b	2b	2c	2c	2c	2c	2d	3а	3а	3а	3а	3а	3а	3а	3а	3а	3а	3а	3а	3a	3а	3b
Figure 1 - Continued		HCV-1	HCV-J	BE90	2TY4	$4\mathrm{TY4}$	HC-J6	HC-JB	NE91	EB12	ARG6	S ARG8	TI O	∏ T983	H NE92	E CHR20	CHR21	W CHR22	JLE TJ	L.I. 26	NE93	NZL13	EB1	EB2	EB3	EB7	BR33	BR34	BR36	T9

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	21	-G-	CCA-CTA-GGA-G-G-TA-GAGTGA-CTAG	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	G-GAGAAT-CCG	GAATAT-CCG	- T - CTG A -		-G-GAATAA-CCG	TGAAATAATCTG	-CGGGGAATGATCCGA-	- AA T'G A'I'CCG - 1'	A-TGGNG-T-NAATCG	CGAGGAATACCGT	AGGGTT-CTGAA	AGTGG-T-G-GTAATTT-CTGGA	-ACAAACG	-G-CACA	CA-TGTT-GC-GTG-GGTAACGAC-A	CA-TGTT-GC-GTG-GACAACGAC-A
Continued 3	SEQ ID		149	0	0	110	-	\vdash	\circ	\circ		\circ	\circ				159	9		
		3b	30	4 c	4 C	4 C	4 C	4 e	4 e	4 £	49	4 h	4 i	4 j	4 k	4 k	5a	5а	5a	5a
Figure 1 -		T10	BE98	GB48	GB116	GB215	GB358	GB809	CAM600	S CAMG22	드 GB549	F GB438	CAR4/12	TCAR1/501	N EG-13	T EG-19	S BE 3 2 5	BE96	CHR18	CHR19

1 - Continued 4	## ## ## ## ## ## ## ## ## ## ## ## ##	3a
Figure 1 - Contin	HCV-1 HCV-1 HCV-1 BE90 2TY4 4TY4 4TY4 11 4TY4 11 HC-J8 22 HC-J8 NE91 NE91 22 22 23 23 24 14 15 16 25 26 27 27 27 27 27 27 27 27 27 27	

Figure 1 - Continued 5

CGCA-CTCA-GTACAGT-ACTCC-G CCTGTTA-GTTCAGC-AAC-AC	ACCGCTCA-GCATCAGC-AACCTGACGCTCA-GCATCAGC-AACCTGACGCTCA-GCATCAGC-AACCTGACCGCTCA-GCATCAGC-AACCTGTACCGC
3b 3c	4 4 4 4 4 4 4 4 4 6 6 6 6 6 6 6 6 6 6 6
T10 BE98	GB48 GB116 GB215 GB215 GB358 GB809 CAM600 CAM622 CAM71/501 CAR1/501 CAR1/501 CAR1/501

Continued 6	### ##################################
Figure 1 - Continued	HCV-1 HCV-1 BE90 2TY4 4TY4 4TY4 HC-J6 HC-J6 HC-J8 NE91 I10 NE92 CHR20 CHR20 CHR21 CHR21 EB2 EB2 EB3 EB3 BR34

ontinued 7	8082 3bTC-CCTC-TC-TCT	G G
- C01	3b 3c	15 15 15 15 15 15 15 15 15 15 15 15 15 1
Figure 1 - Continu	T10 BE98	GB48 GB116 GB116 GB215 GB215 GB358 GB358 GB438 GB549 GB549 GCAR4/120 GCAR1/501 BE95 GCHR18 CHR18

inued 8	8132 CCCTCACTTGCTACATCAAGGCCCGGGCAGCCTGTCGAGCCGCAGGGCTC	AT-GACTGTAA	TATC-ATCTT-TGAA		1	W:::::::::::::::::::::::::::::::::::::	GATAG	GGTA	GA	-GATAAAGAAACG	-GAAGGAACG	-GAA-AGGAACG	-GAAAGCAACTGCA	GG-GA-AAAAGT'GCA	TTTA-A-AGI-CGAAG	TTGCGAAG		TT	TAUAG	-GGCGAAG	TACAGTGC-AAGA	TT	T	and the second s			THE PROPERTY OF THE PROPERTY O	AC-WAMA	- AA-ACTACTA-CA-GI
- Cont	<u></u>	1b	1b	10	10	2a	5p	2b	2b	2c	2c	2c	2 C	2 q	3а	3а	За	3а	3а	3а	3а	3а	3а	3а	3а	3а	3a	3а	3b
Figure 1 - Conti	HCV-1	HCV-J	BE90	2TY4	4TY4	HC-J6	HC-J8	NE91	EB12	S ARG6	ARG8	110	S T983	S NE92	哥 CHR20	CHR21	CHR22	LI LE:	LL 26)	NE93	NZL13	EB1	EB2	EB3	EB7	BR33	BR34	BR36	7.9

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Figure 1 - Contin	Contir	ued 9
		8181
	3b	ACTACTGA-CA-GTGT
BE98	30	-C-
B4	4 C	-AGGCG
GB116	4 C	-AGGTCATCACTATCAGGG
GB215	4 C	TCATCACATCA-G-
GB358	4 c	-AGGGCG
GB80	4e	-AA-GGC-TTCAATCA-GTGA
	4e	-AGGGC-TATCAATCA-GTG
T28	4 £	-TGGT-CACAGACCAATCA
	4g	-TG-AGTTCGTTGTAC-A-GTG
	4 h	-GG-GAC-TAACAACCA-GTG
CAR4/	4 i	-GG
CAR1/5	4]	-AGGCC-TACATTAC-AACCT-A
N EG-13	4 k	-GGGC-AAACCTAT-AGGG
TEG-19	4 k	-GGGCCACACTAT'-A-GGAA
S BE95	5а	A-GGATTACTAA
BE9	5a	A-GGTT'I'I'AC'I'\TT
CHR18	5а	A-GG
CHR19	5a	A-GG

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- Continued 10	8231	a CAGGACTGCACCATGCTCGTGTGGCGACGACTTAGTCGTTATCTG	b	q	1c		ATT-CGCCAGACTGTC	d	b GTCC-GTG	b GT	c GTT-	c GTT-	c GTT	C GTT-CT-C	d ATT-C-CCGGGG	a -G-ACCGGA-T-TTCCATTC-G-	3 G-AC-CCGGA-T-TCCAT-T-G-G-G-G-CATTG-G-G-G-G-CATTG-G-G-G-G-G-G-G-G-G-G-G-G-G-G	AG-ACCGGA-T-TTCCCTTC-G1GG-GGC	B -G-ACCGGA-T-TTCCAIC-G	a -G-ACCGGA-T-TTTTG-GC	8	a -G-ACCGGA-T-TTCCATTGGGC-	a -G-A-T	a -G-A	a -G-A	-G-ACCGGA-	8 - G-ACCGGA-T-T'T'T'T'TGG-GGC	a -G-ACCGGA-T-TTCA11C-CA	ATTC-GG-A-C	A = A - A - A - A - A - A - A - A - A -
Figure 1 -		HCV - 1	HCV-J	BE90	2TY4	4 T Y 4	HC-J6	HC-J8	NE91	EB12						CHR2	CHR2	E CHR22	T1			NZL13	EB1	EB2	EB3	EB7	BR33	BR34	BR36	$^{\mathrm{T9}}$

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inued 11	A-ACCATT-CTCCATGGG-G-C	A-AA-TCCAT-AT-CTCCATGGTGC	AGA	DD-D	- L C - G C -	- L C - G	-TCT	D	A	GT	GAC'I	- 1	A-AT	AGA T		TC-T	CGTTCATG-	CGTTTTG-CCT	
- Continued	3p	30	4 c	4 C	4 C	4 C	4 e	4 e	4 £	49	4 h	4 i	4]	4 K	4 k	5а	Ба	5а	5a
Figure 1 -	-	BE98	GB48	\vdash	GB215	GB358	GB80			GB54	m GB438	CAR4/12		(R) EG-13	EG-	Щ	BE96	CHR18	CHR19

1 - Continued 12	8232 8271	1a AAGCGCGGGGGTCCAGGAGGACGCGGCGAGCCTGAGAGCC	1b GTAACTGCAC	1bAACA	2a GCAAC-GA-CGA	2b GCAATAA-GA-CGA-AT	2b GCATAA-GA-CGA-AT	2d GTCAAC-GA-CGAAC	3a GT-ATCG-CTAGAAGC	1 1 1 1 5 5	3a GT-ATCA-TTAGAAGCG	3a GATCG-TTAGAAGC	3a GT-ATCG-CTAG-AGC	3a GT-ATCG-CTAGAAGC	3a GT-ATCG-TTAGAAGC	ı	3a GT		TGCCGAGAAGCT	3bTGCCGAGAAGCTC	3c GTAG-TAGA
Figure 1 -		HCV - 1	HCV-J	BE90	HC-J6	HC-J8	NE91	NE92	CHR20	G CHR21	S CHR22	S T1	T 7	E NE93	NZL13	IN BR33	m BR34	6 BR36	T9	T10	BE98

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Figure 2		GEO 10	2694
HCV - 1	la		TVTESDIRTEEAIYQCCDLDPQARVAIKSLTERLYVGGPLTNSRGENCG
HCV-J	$^{1}\mathrm{p}$		SA-EQR
BE90	1b	214	A-E H-D
4 T V 4	ט נ		NAU-H
+	4		;
HC-J6	2a		RA-S-PEE-HTHMF
HC-J8	2p		A-S-PQETV-H
NE91	2b	216	-S-PQETV-HMI-
EB12	2b		S-PQETV-H
ARG8	2c		S-PEG-T-HHTBEG-S
110,	2c		-WHIS-
T983	2c		A-S-PQETHH
NE92	2d	146	RSLA-S-PETHMLK-QT
CHR20	3 a		S
CHR21	3a		QWFK-AQ
CHR22	3a		QVEN-E-EKV-SCMFK-AQ
TI	3а		SMF
T.7	3а		-EKV-SCMY
NE93	3а	218	N-E-E-KV-SCMF
NZL13	3а		-E-EKV-SC
EB1	3а		-E-EKV-SK-AQ-
EB2	3a		-E-E-KV-SCMFK-AQ-
EB3	3а		-E-E-KV-S
EB7	3а		MFK-AQ-
BR33	3a	10,12	MFK-AQ-
BR34	3а	2,4	QK-X QK Q
BR36	3а	6,8	- C
T9	gę.		- T E - E - E E
T10	3p	,	**************************************
BE98	3c	150	15/

Figure 2 - Continued 1

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2694	K-DL	K-DL	K-DI,	DI'	K-DI	K-DL	K-DI,	K-DL	DT	K-DL	K-DL	K-DL	K - DL	K-QQ	K-QQ	K-00 K-00
						 	! ! !	1 1 1		MY-	KMY		ī I	CMY	-FCMY]	CMY
2645	VN-E-EKTA	VS-ELEKV-TA	KVEVE-E-KTA	KTA	KVEVE-E-EKV-TA	E-ETA	E-EKV-AA	1 1	RVEVE-ET-KV-SA	ı	RVEE-EKV-SA	PR-X-VEVN-EXDX-KV-NA	X-RGEVE-EKV-TA	HMSQ-EARQ-	AHLSSQ-DARQ-	HMSSLY-Q-ERQCMYK-QQ HMSSLY-Q-EARQCMYK-QQ
			107	109	111	113	117	202	204	115	208	210	212	9	9	
	4 a		4 C °	4 C	4 C	4 C	4 e	4e	4 £	4g	4h	4 j	4 j	5a	5а	5а 5а
	EG13	EG19	GB48	GB116	GB215	GB358	GB809	CAM600	CAMG22	GB549	GB438	CAR4/1205	CAR1/501	BE95	BE96	CHR18 CHR19
		2645 VN-E-EKTAMHK-DL-	2645 4a	4a VN-E-EKTAMHK-DL- 4a VS-ELEKV-TAMIIK-DL- 4C° 107	4a VN-E-EKTAMHK-DL- 4a VS-ELEKV-TAMHK-DL- 4c 107	4a VN-E-EKTAMHK-DL-VS-ELEKV-TAMHK-DL-V	4a VN-E-EKTAMHK-DL-V	4a VN-E-EKTAMHK-DL-VMHK-DL-V	4a VN-E-EKTAMHK-DL- 4a VS-ELEKV-TAMHK-DL- 4c 107KVEVE-EKTA	4a VN-E-EKTAMHK-DL-V	4a VN-E-EKTAMHK-DL-V	4a VN-E-EKTAMHK-DL-V	4a VN-E-EKV-TAMHK-DL-V	4a	4a VN-E-EKTAMHK-DL-VS-ELEKV-TA	4a 4a VN-E-E-K-TAMHK-DL- VS-ELE-KV-TAMHK-DL- 4c 109 VS-ELE-KV-TA

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GB48 GB116 GC		A	A	A	A	A	AA	A	1 1 1	A	A-	S -			N	- H - A	A	- VTA	
GB48 GB116 GB215 GB358 GB358 GB809 CAM600 CAM622 GB549 GB741205 A GB71/501 A GG13 A GG19 A	695	YRIJSIKR	YFLSI	YFY-	YRR		KK	YKFLTKK	YKG-S	YKK	YK			YFK-	R-R-RII-SR-II	RRML-STR-Y-L	KKKL-SKL		
GB48 GB116 GB215 GB358 GB809 CAM600 CAM622 GB549 GB438 CAR1/12 CAR1/50 EG13 EG13 EG19 BE96 CHR18			4c	4c			4e	4 £	4g	4 h	4 i	4 j	4 K	4 k	5а	5a	Sа		
		GB48	GB116	GB215	GB358	GB809	CAM600	CAMG22	GB549		CAR4/12	CAR1/50							;)

Figure 2 - Continued 3

2 - Continued 4

luea 4	2745 SAGVQEDAASLRA	T	V	-Q-TEERN	1	1	-Q-TEERN	- D D R - A	- D D RTA	-DNR-A-G-	-DDR-A	-DDRTA	-DDR-A	-DDR-A	1	i		- R -	띰	IDR-
- Continued	1a	1b	1b	2a	2b	2b	2d	3а	3а	3а	3а	3a	3а	3а	3a	3а	3а	3b	3р	3c
Figure 2	HCV-1	HCV-J	BE90	HC-J6	HC-J8	NE91	NE92	CHR20	CHR21	CHR22	T1	T7	NE93	NZL13	BR33	BR34	BR36	T9	T10	BE98

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1	ATGAGCACGAATCCTAAACCTCAAAAAAAAAAAAGGTAACGTAACGACCG				- W - W	- Т W - W)) t 			51	CGCCCACAGGACGTCAAGTTCC			_	(O) W)1,	-	
SEO ID				143				4	191	9	9	9		151																
	1a	αŢ	2 K	2d	3а	3а	3b	30	4 C	4 e	4 e	4.2	4.2	5а		1a	1p	2a	2 b	2d	3а	За	3b	3с	4 C	4e	4 e	4.5	4 ?	5a
Figure 3	HCV-1	HCV - J	HC-16	NE92	EB1	NZL1	HCV-TR	BE98	GB358	GB809	CAM600	GB724	EG-29	BE95		HCV - 1	HCV-J	HC-J6	HC-JB	NE92	EB1	NZL1	HCV-TR	BE98	GB358	GB809	CAM600	GB724	EG-29	BE95

Figure 3 - Continued 1 HCV-1 HCV-1 HCV-1 HCV-3 HC-38 HC-38 HC-38 HC-38 HC-38 HC-38 HC-38 HC-48 HCV-TR HCV-TR HCV-TR HC-78 HC-	CTTGTTGCCGCCCAGGGCCCTAGATTGGCTCTGCGCGCGC
)	G
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4e	
4e	# D D E
4c	
3	BB
3b	CAAACAG
3aA	AAGACA
3aA	AAGCACA
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2b -	
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1p	E C C C C C C C C C C C C C C C C C C C
1a AAGACTT	CGAGCGGTCGCAACCTCGAGGTAGACGTCAGCCTATCCC
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3cG-	C-AACCAGTA(3"'-C
3b -ATG-	CTACAGI'AC
3a -AG)
3a -A)+
2d -A	
2b	CG
2a -A	- W
1bC-	
la TTTA	STTGCCGCCCAGGGGCCCTAGATTGGGTGTGCGCGCGCGAGA
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- Conti	

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Figure 3 - HCV-1 HCV-J HCV-J6 HC-J8	. Continued 2 2 1 1 6 1 5 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	2 01 GCTCGTCGGCCCCGAGGGCAGGACCTGGGCTCAGCCCGGGTACCC' C
EB1 NZL1		GAGAT
HCV-TR BE98		TCGC AA
GB358 GB809		T
CAM600	4 e	1 1 1 1 1 1 1 1 1 ()
EG-29 BE95	4? 5a	GAT
		5.1
HCV-1	1. 1.	CCCTCTATGGCAATGAGGGCTGGGTGGGCGGGATGGCTCCTGTCTCCC
HCV-J HC-J6	15 2a	ACGACTCA
HC-J8	2b	OBC
NE92 EB1	2d 3a	
NZL1	3а	A
HCV-TR		-)
BE98	ພ ວ ເ	TTG
GB809		AG
CAM600	4 e	1
GB724	4?	: -DW
EG-29	4?	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
BE95	5a	

ontinued 3	301 CGTGGCTCTCGGCCCTAGCTGGGCCCCCACACACCCCCGGCGTAGGTCGCG CGTGGCTCTCGGCCTTAGCTGGGCCCCCCCGGCGTAGGTCGCG CA-T-C-T-C-T-C-T-C-C-C-C-C-C-C-C-C-C-C-C	351 CAATTTGGGTAAGGTCATCGATACCCTTACGTGCGGCTTCGCCGACCTCA 1b T
Figure 3 - Co	HCV-1 HCV-J HCV-J6 HC-J8 NE92 EB1 NZL1 HCV-TR BE98 GB809 CAM600 GB724	(95 3708), L33HS HC-J6 HC-J8 NE92 EB1 NZL1 HCV-TR GB809 CAM600

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(x	26/111	
	TTCGCCGACCTCATGGGGTAC	A A A A A A A A A A A A A A A A A A A) U <
	SEQ ID NO	143 13,15,17 23,25,27 19,21 183 183 185 118,187 167 171	7
	7 11 1 1 1 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2	225 332 332 332 332 444 44 46 46 46 46 46 46	49 4h 4i
r Jdnr a	HCV- HCVE HCVH HCVH HCVT HCVT	HC-JB HC-JB HC-JB HD10 BR33 HD10 GB835 GB809 4 GB116 GB358 GB809 2 CAMG22	CAR4) CAR4/1205

Figure 4

CAR4/901 4? 181 BE95 5a 143 BE100 5a 195	GA	AT	
CAR4/901 BE95 BE100	4 ?	5 a	<u>Б</u>
	CAR4/901	BE95	BE100

Figure 4 - Continued 1

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Conti	
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Figure 6	

	478 G									2	8/1	11															
	AGGGCCCTGGCGATGGCGTCCGGGTTCTGGAA			·····[···[····························		***************************************	CAG	ATCGA-AC	CATACT	AGTT-TCATCGA-A	- CC T -		TT-CYTT	-V	-GGT'CAA	Q -	TTC	-GTTCAV	-GTTC	-GTTCAATA	OTTT	TTGAT		-G-GLTTT	()		
	1 a	la	1a	la	1a	٦ ا	1p		2b		3a	3а	3а	3a	3b	4a	4 c	4 C	4 C	4 e	4 e	4 E	4 £	4 g		4 h	41
·	HCV-1		HCVHCT18	\sim 1	HCVHCT27	HCVTH	HCV-J	٦.	HC-J8	(T)	HD10	BR33	BR36	NZL15	HCV-TR	GB809_4	GB116	GB215	GB358	GB809_2	CAM600	CAMG22	CAMG27	GB549		GB438	CAR4/1205

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Continued 5	CG-GTTCA	CGGTCATCACTGACTG- CGGTCATCATGATG-
Concr	4.2	5a Sa
Figure 4:	CAR4/901	BE95 BE100

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ued 5	GA-CTTT	1 (CTT-AC	
Continued	4;	4 ا د ۲۰	5 a	5a
Figure 4 - (CDR4/1205	7901	}	BE100

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inued 6	529 TTCCTTCTGGCCCTGCTCTTGCTTGACTGTGCCCGCTTCGGCCTACCA	T-G
Cont	13 13 13 13	В В В В В В В В В В В В В В В В В В В
Figure 4 : Continued	HCV-1 HCVEC1 HCVHCT18 HCVHCT23 HCVHCT27	HC-J6 HC-J6 NE92 NE92 BR33 NZL15

7	i i	9-91W9KCCCBLKDC	SLC	B-CB		· · · · D · · · · · · · · · · · · · · ·) ;	GT-A-	- Y	L9-9b			T. I.		AATG) }	- G C T	TATGC-CCG-	-
Continued		4a	4a	4 b	4c	4 C	4c	4c	4c	4q	4e	4 e	4£	4 £	49	4 h	.다.	4. ?		กับ บ	
Figure 4 -		GB809_4		Z1	GB116	GB215	GB358	9Z	27	DK13		$CAM60\overline{0}$	G22	G27	GB549		CAR	90	' I	a BEU5 BE100	SA4

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- Continued 8	1a AGTGCGCAACTCCACGGGGCTTTACCACGTCACCAATGATTGCCCTAACT 1aTTTTC 3 1aTTTTTT	2aAAGATGTACCGGCATGGCCA-CTG 2bCA-GATT-GTTCTAGCTT-AA 2c GCAAGGAGGC-ACTCCATGCCGCT-C 2d GCAAGGAGCA-CTCATGCCGCT-C 3a GTGGTA-GT-TCTGT-C-TAGTA 3a GTGGTA-GT-TCTGT-C-T
Conti	11 11 12 12 12 12 12 12 12 12 12 12 12 1	22 22 22 23 24 25 25 25 25 25 25 25 25 25 25 25 25 25
Figure 4 - Conti	HCV-1 HCVEC1 HCVHCT18 HCVHCT23 HCVTH HCVTH	HC-J6 HC-J8 S83 NE92 NE92 HD10 BR33 HCV-TR

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862	TG TT CA - C - T A T - G - T A T - G - T T - T G - T T G - T T G - T T G - T T G - T T G - T T G - T T G - T T G - T T G - T T G - T T G - T T G - T T G - T C G - C C G T T G - T
inued 9	579 CTACG- CTACG- CTAT CTAT CTAT CTAT CTAT CTAT CTAT CTAT CTAT CTACG- CTACG- CTACG- CTACG- CTACG- CTACG- CTACG-
- Contin	ффффффффффффф КССС В в в СССССО в в в ССССССССССССССССССССС
Figure 4 -	GB809_4 24 21 21 GB116 GB215 GB215 GB358 26 27 27 G22 CAM600 G27

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inued 11	629	-CG-ACTAA-T-A-C-CCATAT	ACTAT-ACCA	A AGC - CCA A	T-A-T-CCA	C - A - C - CCA	ACTC-	T-ACTC-	ACTC	T-ACTC	-CAT-A-C-A-ACAT-ACTC-	T-ACTC-	-CAC-TTA-T-CCATCT	-CAC-TTA-AGCCATTCT	-T-A-CCATATCTA	-CAA	.C-AGA-CCATCT	-CCATTAAC-ATC-CCAATTAA	-TTCCACTA-ATA-CCTGAG-ATT	-CLG	-TTCCATT-ATA-CCTGTTG-AT'T
Cont		4 a	4 a	4 b	4 C	4 C	4 C	4 C	4 C	4 d	4 e	4 e	4 £	4 £	49	4 h	4 i	45		5а	
Figure 4 - Contir		GB809_4	24	Z1	\leftarrow	GB215	Ω	92	7.7	Ω	GB809	CAM600	<u>S</u> 622	ਜ਼ G27	GB54	T GB438	CAR4/12	E CAR4/901	BE9	BE100	SA4

<u>ued</u> 12	728 GTCCCTTGCGTTCGTGAGGGCAACGCCTCGAGGTGTTGGGTGGCGATGAC ACT	GAGAAA-TGTA-ATCCA-ACAAG-AT-AGAATAATGG-AT-CATCA-ACAAG-AT-AG-AACC-CT-TC-ACG-TGT-AGGAGAATACC-CA-ACC-G-TTATC-AGCTTA-ATGCCACCC-AG-A A-ATC-AGCTA-AT-CACACCC-AG-A A-ATC-AGCTA-AT-CACACCC-AGATC-AGCTA-AT-CCACCC-AGATC-AGCTA-AT-CCACCC-AGATC-AGCTA-AT-CCACCC-AGATC-AGCTA-AT-CCACCC-AGATC-AGCTA-AT-CCACAAG-CT	
Continu	12 12 12 12 13	222 222 232 232 232 232 232 232 232 232	
Figure 4 - Continued 12	HCV-1 HCVEC1 HCVHCT18 HCVHCT23 HCVHCT27 HCVTH	HC-J6 HC-J8 S83 NE92 HD10 BR36 NZL15 HCV-TR	
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	728	-CGA-G-CCGTGTC-TCAC-CG-A	-CTGATGACTGA-AC-T-	-CTGGACAGTA-TTC-CCC-CT	-CGA-G-TTGTCAGAC-C-	-CTGA-G-TTGTCAGAC-TCC-CT-	-CGA-G-TTGTCAGAC-CCCC-C-	-CTGA-G-TTGTCAGAC-C-	CTGA-G	GA-GAGAAGT-CA-	-GAAGACCGCAGC	CTGA-GACTGCAGC	CAGTCA	TGA-AACTGCAGAC-ACA-	GA-AACCGAC-CC	TAA-AACTGT-TC-TCA-TC-	TGAAGACCGTCAGCC	-CGA-GACCGTTC-CAT-TC	TCATGACATT-TGAGTA-	TCA-GA-A-ATT-TGAGT	T CA - GC - A - AT T - T - AGT - A C CCAA C
cinued 13	679	 	-TGA	- J L -	GA-G-	- T GA - G-	GA-G-	-TGA-G-	- T		ACTGAAGACC	1 [-]		CTGA-AACT	1	ı	- 1	i i I		1	GTCA-GC-A
Cont		4 a	4 a	4 b	4 C	4 C	4 C	4 C	4 C	4 d	4 e	4 e	4 £	4 £	49	4h	4 i			5a	
Figure 4 - Conti		GB809 4	Z4	Z1	B11	B21	35	26	72	DK13	GB809	CAM6	G2		GB	E GB438	CAR4/12	CAR4/901	BE9	BE100	K

	778 TCGAC G	A GA G A G C G C	ACA ACA ACA ACA
nued 14	729 CCCTACGGTGGCCACCAGGGATGGCAAACTCCCCGCGACGCAGCTTCGACC	AG-ATGTGCA-C-GCC-GGCGCT-ACA-GGCT-AGA AC-ACTGTG-AAC-CCGGTGCG-T-A-TCGTAGCGA C-ATC-CTATC-ACCTGGCGCT-T-A-T-A-GGCGG GC-ATA-ATGTGCC-ACCTGGTGCG-TTA-C-A-GGCGGA	AAGTT-C-T-GG-GCAAA-CG-TTC-A-ACA AAGTT-C-T-GGGGCAAA-CG-TTC-A-ACA AAGTA-T-C-T-GG-GCAAA-CG-TTC-A-ACA AAGTA-T-C-T-GG-GCAAA-CG-TTC-A-ACA AAGTT-C-T-GG-GCAAA-CG-TTC-A-ACA AAGTT-C-T-GG-GCAAA-CG-TTC-A-ACA
Contin	1 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	2a 2b 2c 2d	3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3
Figure 4 - Continued 14	HCV-1 HCVEC1 HCVHCT18 HCVHCT23 HCVTH	HC-J6 HC-J8 S83 NE92	HD10 BR33 BR36 NZL15 HCV-TR
		SUBSTITUTE	SHEET (RULE 26)

		ACT-AGCC-AGCCT-GG-GCAGT-AG-T-CTGA CCT-AGCC-AGCTT-GG-GCAGT-AG-T-CCGA CT-AGCC-ACT-GG-GCGGT-AG-T-CTGA
- Continued 15	4a A	5a
Figure 4 - C	GB809_4 Z4 Z1 Z1 GB116 GB215 GB358 Z6 Z7 Z7 GB809_2 GB809_2 G22 G22 G22 G22 G22 G22 G22 G22 G22 G	BE95 BE100 SA4

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<u>ued</u> 16	4 1 1 1 1 1	CGTCAGGAT-TCG'III CAGCAA-CAA'I-GCATGGCC'I'-GT CAGA-CA-CGAT-'I'CTTGGTT'I CA	
Contin	12 12 12 12 13	2a 2b 2c	Д w w w w м м м м м
Figure 4 - Continued 16	HCV-1 HCVEC1 HCVHCT18 HCVHCT23 HCVHCT27 HCVTH	HC-J6 HC-J8 S83 NE92	HD10 BR33 BR36 NZL15 HCV-TR
		SUBSTITUTE S	SHEET (RULE 26)

<u>ed</u> 17	828 -G-TG-G-C-C-AA-G-A-TGCGG-GT-TT -A-TG-GCT-AA-GA-CGCGTT-GT-TT -G-TG-ACA-G-G-TGCG-T-T-TA-GC-T-TTG-GA-GA-TGCTT-TG-GCT-TTTG-GA-GA-TGCTT-TG-GCC-TTTG-GA-GA-TGCTT-TG-GCC-TT	-AGC-G-TCTACA-CGAG-GTGCCGT-A -AGC-G-TTACT-GGAG-GTGCCGT-A -GGC-G-TCTACT-A-CGAG-GTGCCAA
Continued	4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	5 5 8 5 9 8 9
Figure 4 - (GB809_4 Z4 Z1 CB116 GB116 GB215 GB358 Z6 Z7 Z7 Z6 Z7 Z6 Z7 Z6 Z7 Z6 Z7 Z6 Z7 Z7 Z7 Z6 Z7	BE95 BE100 SA4

	878 GTGGGGACCTATGCGGGTCTGTCTTTCTTGTCGGCCAACTGTTCACCTTT-GTTT-GTTT-G	GATGGGGA-GCA-CGATTG- ATG-GG-CGA-GAC-ATCGGGCTTGG- G-GTCG-GC-GA-GG-CCTGG-CGGT-G- AGTCG-GGA-GT-G-CTTCTG-CT-A-	-TTA-GTG-CCCGAGCCG -TTA-GTG-CCCGAGCCG -TA-GTGCCGAGCCG -TTA-GTG
nued 18	829 GTGGGG	A - A	
Conti	19 19 19 19	2a 2b 2c 2d	3a 3a 3b
Figure 4 - Continued	HCV-1 HCVEC1 HCVHCT18 HCVHCT23 HCVHCT27 HCVTH		AT HD10 HBR33 BR36 SPR15 HCV-TR

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	878	1		 	} } 	- LL	1 1	- I,	V T'T A	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	· · · · · · · · · · · · · · · · · · ·	A	1 1 1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 8 1 7	:	T.A -				AA
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inued 19	829	TA	I	A-TAT-	A-C	A-TT	A-CA	TAT-	A-T	A-CAG	C C	ı		- A T -	CA	A	A-TAT-	C A		D A E	C
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Figure 4 -		GB809 4	Z4 _	21	GB116	GB2.15	GB358	26		SBC DK13	GB809			H G27	GB54		CAR4/12			BE95	E T

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879	CTCTCCCAGGCGCCCACTGGACGCAGGGTTGCAATTGCTCTATCTA				C		ATC-CGT-TGAGTAAA	GACAATTTGTAC	AAACAAAACT'TCCAGCTCC-	GGACAA-ATAC-T'TTGTCG-AACTCAC-	GCAATTAA-T'I'I'G'I'CG-ACCTCAC-	-AGATC-TTCAAGTCGACCTCAC-GC-	-AGAC-C-CTCAAGTCGACCTCGC-GC-	TCAAGTCGACCTC	-AGATC-ATCAAGTCGACCTCGC-GC-	-AGATC-CACCGTGACGCGAC-
	1a	1a	1a	la	1a	Тa	$^{1}\mathrm{p}$	2a	5p	2c	2d	3a	3а	3а	3а	3b
	HCV-1	HCVEC1	HCVHCT18	HCVHCT23	HCVHCT27	HCVTH	HCV-J				HE NE92				WNZL15	HCV-TR

	928 A CG CG CG G G	CA CA
<u>ued</u> 21	- C G - A T C - B - A T - C - B - A C G - A C G - A C G - A C G - A C G - A C G - A C G - A C	TAGGTC-C-AGGCTGTGAAC TAGGTC-C-AGTGCTGTG-AC TAGGTC-C-AGACTGTAC
Continu	444444444444 330000000年年 5日よう	2 2 2 3
Figure 4 - Contin	GB809_4 Z4 Z1 GB116 GB215 GB215 GB358 Z6 Z7 Z6 Z7 GB809 Z7 GB809 Z7 GB843 GB549 GB549 GB549 GB549 CAR4/1205	BE95 BE100 SA4

Figure 4 - Continued 22

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HCV-1 HCVHCT18 1a HCVHCT23 1a HCVHCT27 1a HCVTH 1b HCV-J6 2b 2c 2c 2d HC-J8 2b 2c 2d S83 2c 2d S83 S83 S83 S83 SC S83 SC SB3 SC SB3 SC SC SC SC SC SC SC SC SC SC	929	CCGGCCATATAACGGGTCACCGCATGGCA		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		5				-ACTATGG	- A A A T		. A C - 'I'I' - A I A I],V ,VVL-DV-	C-TrT-AAT	OV-IV-I-V-V-I-VV-	
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GODOTITOTE GITEET (NOCE TO)		HCV-1	HCVHCT18	HCVHCT23	HCVHCT27	HCVTH	HCV-J	(_		•	•					

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nued 23	929	-CCA-G	V-G	CG-CTA-	-TA-	C L C G-	-GG-TA-		G CG - T A C A	- A C A A A -)CC		TC-CCTA-AT	l I	1	TCCACA-AT	99	TCG-CCT-A	GT
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Figure 4 -		GB809 4	Z4	\overline{z}_1	GB116	GB215	GB358	92	27	DK13	GB809 2	$CAM60\overline{0}$	G22	G27	GB549	GB438	CAR4/1205	CAR4/901	Ç	おだりら	A4

1 MSTNPKPQKKNKRNTNRRPQDVKFPGGGQIVGGVYLLPRRGPRLGVRATR R-TR-T	R-TR-T		R-T
SEQ ID	144	148	192 164 166 194 152
1a 1b	2a 2b 2d	3a 3a 3b 3c	4c 4e 4? 4? 5a
HCV1 HCVJ	HCJ8 HCJ8 NE92	EB1 NZL1 HCV-TR BE98	GB358 GB809 CAM600 GB724 EG-29 BE95

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		PGYPWPLYGNEGCGWAGWLLSP M				
	V-core	RPEGRTWAG	-ST-KS-GK -ST-KS-GK T-KS-GK	- S S S S	· · · · · · · · · · · · · · · · · · ·	Q-TS-G-
nued 1	51	KTSERSAPRGRRAPIPKAR RPEGRTWAA				
· Continued 1		1a 1b	2a 2b 2d	3a 3a 3b 3c	4c 4e 4? 4?	5a
Figure 5		HCV1 HCVJ	HCJ8 HCJ8 NE92	EB1 NZL1 HCV-TR BE98	GB358 GB809 CAM600 GB724 EG-29	BE95

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nued 2	101 126	RGSRPSWGPTDPRRRSRNLGKVIDTL		NHN	I K I	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	· · · · · · · · · · · · · · · · · · ·	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	· · · · · · · · · · · · · · · · · · ·	· · · · · · · · · · · · · · · · · · ·	- X X N X X -	1	· · · · · · · · · · · · · · · · · · ·
· Cont		<u>1</u> a	1b	2a	Sp	2d	3a	3b	3с	4e	4 е	45	, 5a
Figure 5 · Continued 2		HCV1	HCVJ	HCJ6	нслв	NE92	NZL1	HCV-TR	BE98	68889	CAM600	GB724	BE95

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17K	127 TCGFADLMGYIPLVGAPLGGAARALAHGVRVLEDGVNYATGNLPGCSFSI		
Continued 3	<u>6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 </u>	2a 2b 2d	3a 3a 3b
Figure 5 -	HCV-1 HCVEC1 HCVHCT18 HCVHCT23 HCVHCT27 HCVTH	HC-J6 HC-J8 NE92	HD10 BR33 BR36 NZL1 HCV-TR

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5 - Continued 4	127	ta	4cAVI-			IAVI		- 4t	S 4 [†]	6 ₇	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	! †		. 5a
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Figure 5 -		GB809 4	GB116	GB215	GB358	GB809 2	CAM600	CAMG22	CAMG27	GB549	GB438	CAR4/1205	CAR4/901	BE95

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	226	U		1 1 1 1 1
		_PG	1 1 1 1	
	٧2	TNDCPNSSI VYEAADAILHT	TWALA-VV TWALTVL -WALEG-V	D-V A D-V A D-V
	E1	YQVRNSTGLYHV S HS-1 S-1	I-T-V AE-K-ISTG-M- VV VEISSS-YA VE-KDTGDS-MP VE-K-TSSS-M-	FIHAS LEWTSVL FIHAS LEWTSVL FIHAS LEWTSVL FG LEWTSVL
uned 5	177	FLLALLSCLTVPASA YQVRNSTGLYHVS H H	9-AI	
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Figure 5 · Continued 5	,	HCV-1 HCVEC1 HCVHCT18 HCVHCT23 HCVHCT27 HCVTH	HC-J6 HC-J8 S83 NE92	HD10 BR33 BR36 NZL1 HCV-TR

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9 pan ı	177	S	
Contin		649 640 640 640 640 640 640 640 640	6 a
Figure 5 · Continued 6		GBB09_4 Z4 Z1 GB116 GB215 GB215 GB258 Z6 Z7 DK13 GB809_2 CAMG22 CAMG22 CAMG27 GB549 GB549 GB438 CAR4/1205 CAR4/1205 SA4	IIK2

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276	PUTATIVE	VPC VREGNASRCWVAM TPTVA TRDGKLPATO LRRHID LLVGSATLCSALY	# E	1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	IV-	MV-M	MI-MAA		TIIAF	V-YVGATTAS IV- MAM	V-YVGATTAS I-S-VAM		WV	I - T - V - M ARQ
	_	LRRHID	! ! !	1 1	! ! ! !	1 1 1 1		1 1 1 1	-V-T	V		- ^ I	I - S - N-	- N - S - I	- N-S-I	- ^ - I - I
	74	TRDGKLPATQ	1 1 1 1 1 1 1		1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -	RT	A-NSSI-T-T	S-N VQQPGALTQG T	VKHRGALTRS	ISapgaltkg	VSQPGALTKGT	V-YVGATTAS	V-YVGATTAS		V-YVGATTAS	V-TLGVTTAS
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	٧3	VREGNASRCWVAM	\\H-	\\\\\\\\-	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	1	7S-E	FKV11PV	ENDNGTLHIQVN VKHRGALTRS	E-TA-VPV A-NL-	EEKIIPV S-NI-	-QDT-ATPV		-ab1-1-1PV	-dDT-TDD-	-110-S11V ST
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Contin		<u>a</u>	a	, a	_ _ _	<u>. c</u>	1b	2	2b	2c	5d	3a	3a	3a	3а	3b
Figure 5 - Con		HCV-1	HCVEC1	HCVHCT18	HCVHC1 Z3	HCVTH	HCV-J	HC- 14	HC - J8	S83	NE92	HD 10	BR33	BR36	NZL1	HCV-TR

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Figure 5 -	GB809_4 24 21 21 GB116 GB215 GB215 GB358 26 27 DK13 GR809_2 CAM600 CAM622 CAM627 GB549 GB438 CAR4/1205	BE95 BE100 SA4	HK2

	319	CNCSIYPGHITGHRMA			
	٧5	SPRRHWTTQG	0-A-34	QHFV-D QNFE QH-KFV-D	
6 panu	277 TRANSMEMBRANE DOMAIN	VGDLCGSVFLVGQLFTF SPRRHWTTQG CNCSIYPGHITGHRMA		G-M-AA-M-IV VA-MILS-A-MV VALM-AA-VVVV IA-M-AS-V-II	MA
Conti		<u>1 </u>	1a 1a 1b	2a 2b 2c 2d	3a 3a 3a 3b
Figure 5 · Continued 9		HCV-1 HCVEC1 HCVHCT18	HCVHCT23 HCVHCT27 HCVTH HCV-J	HC-J6 HC-J8 S83 NE92	HD10 BR33 BR36 NZL1 HCV-TR

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Figure 5 · Continued 10		GB809_4 Z4 Z1 GB116 GB215 GB215 GB358 Z6 Z7 DK13 CAM600 CAM622 CAM627 GB549 GB438 CAR4/901	ne95 ne100 SA4	IIK2

8077	4648 GTGTGCCAGGACCATCTTGAATTTTGGGAGGCGTCTTTACAGGCCTCACT
ב וחחו ב	HCV-1 HCV-1 HCV-1 HCC 153 HCC-18 HCV-1 EB2 HCV-1 EB2 EB1 HCC-16 EB2 EB2 EB3 EB3 EB3 EB3 EB3 EB3 EB3 EB3 EB3 EB3

Figure 6

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Figure 6 - continued 1	
	4800
HCV-1	CCTTACCTGGTAGCGTACCAAGCCACCGTGTGCGCTAGGGGCTCAAGCCCC
HCV-J	
HC-J6	G-AT-AACCGTACA
HC-18	G-GTAACGCGAAACAA-G
HCC153	T-G-TACTCTTACTACT-C-C-CACTTT
EB1	T-GAACTCTT
EB2	T-GAACTCTT
EB6	T-GAACTCTTCC-CGU
EB7	T-GAACTCTTCC-CGGI
	4849
•	4001
HCV-1	TCCCCAI CGI GGGACCAGAI GI GGAAGI GI I I AAI I CGCCAI CAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG
HCV-J	VV
HC-J6	CGCGTC
HC-18	
HCC153	AGTGAGT
EB1	-VAGT
EB2	AGTGCAAA
EB6	AGTAGT
EB7	AGTGAAC-CG-GGA-

CCCTCCATGGGCCAACACCCCTGCTATACAGACTGGGCGCTGTTCAGAAT ----GAC---T--C--C-----C--C-CT----T--C-GACC---A--A----GC----C--A----V--J--C--A---C--A---C--A--4878 -A--A----A--T--G----T -A--A--C--A--T--G----1 -A---GTG--C--C---T 4850 Figure 6 - continued 2 읝 SEQ ID 29 33 35 37 39 BR36-20-166 BR36-20-164 BR36-20-165 HD10-1-25 HD 10-1-3 HCC153 HC-J6 HC-JB HCV-J HCV-1 EB1 **EB2** EB6 EB7 SUBSTITUTE SHEET (RULE 26)

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Figure 6 · continued 3	4949 4901 GAAATCACCCTGACGCACCCAGTCACCAAATACATCATGACATGCATG	4950 GGCCGACCTGGAGTCGTCACGAGCACCTGGGTGCTCGTTG T
Figure 6 .	HCV-1 HCV-J HC-J6 HC-J8 HCC153 HD10-1-25 HD10-1-3 BR36-20-164 BR36-20-165	HCV-1 HCV-3 HC-36 HC-18 HCC153 HD10-1-25 HD10-1-3 BR36-20-164 BR36-20-165

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continued 4	4991 GCGGCGTCCTGGCTGCTTTGGCCGCGTATTGCCTGTCAACAGGCTGCGTGATGCCA-GAGGT	-AG	5041 GTCATAGTGGGCAGGGTCGTCTTGTCCGGGAAGCCGGCAATCATACCTGAT
Figure 6 -	HCV-1 HCV-J HC-J6 HC-J8	IID 10-1-27 IID 10-1-3 BR36-20-164 BR36-20-166 BR36-20-165	HCV-1 HCV-J HC-J8 HC10-1-25 HD10-1-3 BR36-20-166 BR36-20-166

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Figure 6 - Continued 6

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5191 AAGGCCTCGGCCTCCTGCAGACCGCGTCCGGTCAGGCAGAGGTTATCGCGAT-GCAATAAAACC-GCTATAAT-AT	5241 CCCTGCTGTCCAGACCAACTGGCAAAACTCGAGACCTTCTGGGCGAAGC T - C - TG GG - T G G - G - G
HCV-1	HCV-1
HCV-J	HCV-J
HC-J6	HC-J8
HC-J8	HC-J8
HD10-1-25	HD10-1-25
HD10-1-3	HD10-1-3
BR36-20-164	BR36-20-164
BR36-20-166	BR36-20-165

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Figure 6 ·		HCV-1	HCV-J	HC-16	HC-J8	HD10-1-25	HD10-1-3	BR36-20-164	BR36-20-166	BR36-20-165

1290 1300 1310 1320 1330	1TTGSP1TYSTYGKFLADGGCSGGAYD111CDECHSTDATS1LG1GG	1340 1350 1360 1370 1380 TVLDQAETAGARLVVLATATPPGSVTVPHPNIEEVALSTTGEIPFYGKAI	1 2 1 1 1 1 1 1 1 1 1 N 1 1 1 1 1 1 1 1		N
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	1a 1b 2a 2b 5a	-	10	2a 2b	5a
Figure 7	HCV-1 LCV-1 LCV-1 HC-16	SHEET (RULE 2		HC-J6 HC-J8	BE95

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O _N	1490 1500 1510 1520 1530 AVSRTQRRGRTGRGKPGIYRFVAPGERPSGMFDSSVLCECYDAGCAWYEL	1/111	1540 1550 1560 1570 1580	PVCQDHLEFWEGVFTGLTH	1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	D	
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	1730				
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	1710	NS			- 5!!!!≻
			MEEC	1760	ETFWAK -V /-Q -Q -AH-
	1700		YREFDE -Q -EA -EA	1750	TNWAKI SSK-RA- AS-P-V SS-P
	1690	NS4-1	KPA11PDREVLYREFDE RV		EVIAPAVQTNWQKLETFWAKH -AAV-ESK-RAV QD-QAS-P-V-Q QD-QI-SS-PQ AE-I-TA-H
	16	2	L SG	1740	ALGLLQTASRQA
nued 4			VIVGRVV 11 C-1LH S-1LH HIE A11	NS4-7	ALGLLQ
· Continu			1a 1b 2a 3a 5a		1a 1b 2a 3a 5a
Figure 7 · Conti			HCV-1 HCV-J HC-J6 HC-J8 BR36 BE95		HCV-1 HCV-J HC-J6 HC-J8 BR36 BE95

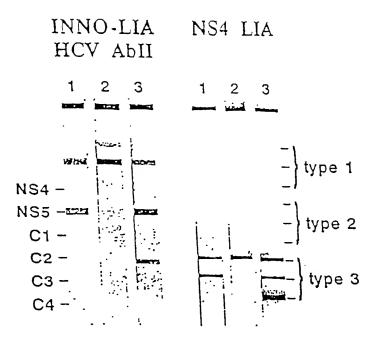


Figure 8

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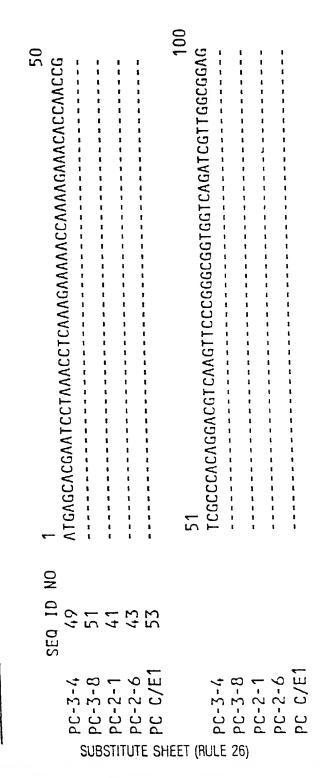


Figure 9

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Figure 9 . Continued 1	101 TTTACTTGTTGCCGCGCAGGGGCCCTAGGATGGGTGTGCGCGCGC	151 AAGACTTCGGAACGGTCGCAACCCCGTGGACGGCGTCAGCCTATTCCCAA
Figure 9	PC-3-4 PC-3-8 PC-2-1 PC-2-6 PC C/E1	PC-3-4 PC-3-8 PC-2-1 PC-2-6

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Figure 9 - Continued 2	250 GGCGCCCACGGGCCGGTCCTGGGGTCAACCCGGGTACCCTTGGC	300 CCCTTTACGCCAATGAGGGCCTCGGGTGGGCAGGGTGGCTCTCCCCCT
Figure	PC-3-4 PC-3-8 PC-2-1 PC-2-6 PC-2-6	PC-3-4 PC-3-8 PC-2-1 PC-2-6

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Figure 9 - Continued 3	301 CGAGGCTCTCGGCCTAATTGGGGCCCCAATGACCCCCGGCGAAAATCGCG	400 TAATTTGGGTAAGGTCATCGATACCCTAACGTGCGGATTCGCCGATCTCA
Figure 9	PC-3-4 PC-3-8 PC-2-1 PC-2-6 PC c/E1	PC-3-4 PC-3-8 PC-2-1 PC-2-6 PC C/E1

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Figure 9	3	CCGCTCGTAGGCGGCCCCATTGGGGGCGTCGCAA
PC-3-8	1 1 1 1 1 1 1 1 1 1 1 1 1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
PC-2-6	1 1 1 1	
PC-4-1	1 1 1 1 1 1	
PC C/E1	1 1 2 1	
7-2-Jd	SEQ ID NO	451 CTCGCACACGGTGTGAGGGTCCTTGAGGACGGGGTAAACTATGCAACAGG
PC-3-8		! ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! !
PC-2-1		
PC-2-6		
PC-4-1	45	
9-4-0d		
PC C/E1		

· Continued 5

Figure 9

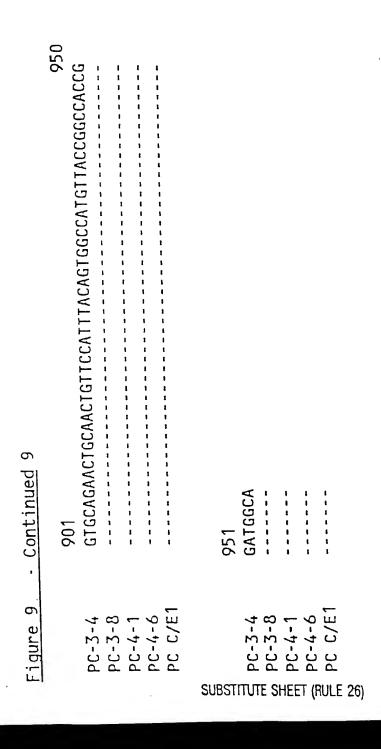
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550 GAATTTACCCGGTTGCTCTTTCTCTTTATTCTTGCTCTTCTCGGT GTCTGACCGTTCCGGCCTCTGCAGTTCCCTACCGAAATGCCTCTGGGATT 501 PC-3-4 PC-3-8 PC-2-1 PC-4-1 PC-4-6 PC C/E1 PC-4-1 PC-4-6 PC C/E1 PC-3-4 PC-3-8

TATCATGTTACCAATGATTGCCCAAACTCTTCCATAGTCTATGAGGCAGA TAACCTGATCCTACACGCACCTGGTTGCGTGCCTTGTGTCATGACAGGTA Continued 6 651 Figure 9 PC-3-4 PC-3-8 PC-4-1 PC-3-4 PC-3-8 PC-4-1 PC-4-6 9-4-Jd

Figure 9 PC-3-4 PC-3-8 PC-4-6 PC C/E1 PC-3-4 PC-3-4 PC-3-4 PC-4-1	Figure 9 · Continued 7	701 ATGTGAGTAGATGCTGGGTCCAAATTACCCCTACACTGTCAGCCCCGAGC	800 CTCGGAGCAGTCACGGCTCCTCTTCGGAGCCGTTGACTACCTAGCGGG
	Figure 9	PC-3-4 PC-3-8 PC-4-1 PC-4-6 PC C/E1	PC-3-4 PC-3-8 PC-4-1 PC-4-6

Figure 9 · Continued 8	801 AGGGGCTGCCCTCTGCTCCGCGTTATACGTAGGAGGCGCGTGTGGGGCA	900 CTATTCTTGGTAGGCCAAATGTTCACCTATAGGCCTCGCCAGCACGCTACG
Figure 9	PC-3-4 PC-3-8 PC-4-1 PC-4-6 PC C/E1	PC-3-4 PC-3-8 PC-4-1 PC-4-6



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	3856 ACCACTGGCAGCCCCATCACGTACTCCCACCTACGG	3940 CAAGTTCCTTGCCGACGGCGGTGCTCGGGGGCGCTTATGACATAATAA	3941 TTTGTGACGAGTGCCACTCCACGGATGCCACATCCTTGGGCATCGGC -ATATGGTCT-CTAA -ACTATGGTCT-TCAA -ACTATAGTCTCTA -AC
	1a 1b 2a 2b 5a 5a	11 12 13 13 13 13 13 13 13 13 13 13 13 13 13	1 1 1 1 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
Figure 10	SEQ ID NO HCV-1 HCV-J HC-J6 HC-J8 PC1 37 197 C1 48 199 BR36 222	SHCV-1 SHCV-J SHCV-J SHC-J8 SHC-J8 SHC-J8	HCV - 1 HCV - J HC - J6 HC - J8 PC1 37 PC1 48 BR36

inued 1	4040 ACTGTCCTTGACCAAGCAGACTGCGGGGGCGAGACTGGTTGTGCTCGC AG-T-GA	4041 CACCGCCACCCTCCGGGCTCCGTCACTGTGCCCCCATCCCAACATCGAGG	4140 AGGTTGCTCTGTCCACCACCGGAGATCCCTTTTTACGGCAAGGCTATC -AGCATTACGCTGGTCA-GAGTTG-GGTGCTGGTCA-GAGGGTTTGCTGGTCA-GAGGGCT
0 - Conti	11 11 12 12 13 13 13	- 11 12 23 53 33	1a 1b 2a 2b 5a 3a
Figure 10 - Contin	HCV-1 HCV-J HC-J6 HC-J8 PC1_37 PC1_48 BR36	HEV-1 HEV-1 HE-J6 HE-J8 HE-C1 HBR36	92 371 92 4CV - 1 92 - 16 92 - 18 92 - 18 92 - 18 92 - 18

tinued 2	4141 CCCCTCGAAGTAATCAAGGGGGGGAGACATCTCTTCTTCTGTCATTCAAAA-TG-CC	4191 GAAGAAGTGCGACGAACTCGCCGCAAAGCTGGTCGCATTGGGCATCAATGTGGGGCCTCGG-GTAT-GCATGAGGCCTCGG-GTAT-GCAATTAAGC-AAC-AGCCG-G-CAATTAAGC-AAC-AGCCG-GC-	4241 CCGTGGCCTACTACCGCGGTCTTGACGTGTCCGTCATCCCGACCAGCGC -TAGTAGCTAAATCAGA -ATATA-GCCTAATCAAAATTA-ACC
Cont	12 12 23 52 32 32	11a 22a 3a 3a	11 22 33 33
Figure 10 - Contin	HCV-1 HCV-J HC-J6 HC-J8 PC1_37 PC1_48 BR36	SHCV-1 SHCV-J SHCV-J TATHC-J6 TAHC-J8 TAPC1_37 TPC1_48	(92 37 HCV - 1 HCV - J HC - J6 HC - J8 PC1 _ 37 PC1 _ 48

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Continued 3	4291 GATGTTGTCGTGGCAACCGATGCCCTCATGACCGGCTATACCGGCGA 1bCCT	4341 CTTCGACTCGGTGATAGACTGCAATACGTGTCTCACCCAGACAGTCGATT 1bTACCGTAGCGTAGTTAC- 2aTCCTGTTGCATTTTC- 5bTTTTCTCTT-CGCCTGGC- 5aTTTTC	4391 TCAGCCTTGACCCTTCACCATTGAGACAATCACGCTCCCCCAGGAT 1b
Figure 10 - Continued	HCV-1 HCV-J HC-J6 HC-J8 PC1_37 PC1_48 BR36	HCV-1 HCV-J HC-J6 HC-J8 PC1 37 PC1 48 BR36	D
		SUBSTITUTE SHEET (RULE 26)

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nued 4	4441 GCTGTCTCCCGCACTCAACGTCGGGCAGGACTGGCAGGGGAAGCCAGGGGGTG-GGAT	4491 CATCTACAGATTTGTGGCACCGGGGAGCGCCCCTCCGGCATGTTCGACTGA-TAAAAAAAAAA	4551 CGTCCGTCCTCTGTGAGTGCTATGACGCAGGCTGTGCTTGGTATGAGCTC -C-GGC
- Conti	11 22 23 33 33	11 22 33 33 33	1.2 2.2 2.2 2.2 3.2 3.2 3.2 3.2
Figure 10 - Contin	HCV-1 HCV-J HC-J6 HC-J8 PC1_37 PC1_48 BR36	STANDARD HCV-1 HCV-1 HCV-1 HCV-1 HC-J6 HC-J8 HC-J8 HC-J8 HC-J8 HC-J8 HC-J8 HC-J8	92 HCV-1 HCV-J HC-J6 HC-J8 PC1_37 PC1_48

inued 5	4591 ACGCCCGCGAGACTACAGTTAGGCTACGAGCGTACATGAACACCCCCGGTT-GGTC-ATAAAAGCCCCATATATT	4641 GCTTCCGGTGTGCCAGGACCATCTTGAAATTTTGGGAGGCGTCTTTACAG -T-GA
0 - Conti	1a 1b 2a 2b 5a 3a	11 12 12 13 13 13 13 13 13
Figure 10 - Conti	HCV-1 HCV-J HC-J6 HC-J8 PC1_37 PC1_48 BR36	HCV-1 HCV-1 HCV-7 HCY-78 HCY-1 HCY-1 HCY-1 HCY-1 HCY-1 HCY-1 HCY-1 HCY-1 HCY-1 HCY-1 HCY-1 HCY-1 HCY-1

Figure 10 - Continued 6	1a GAGAACCTTCCTTACCTGGTAGCGTACCAAGCCACCGTGTGCGCTAGGGC 1bCC	1a TCAAGCCCCTCCCCCATCGTGGACCCAGATGTTTGATTCGCC 1bGTATGTC	1a TCAAGCCCACCTCCATGGGCCAACACCCCTGCTATACAGACTGGGCGCT 1b -AAGTCGT 2aATAGTGCCCGC-C-CTT 2bATAGACTCGC-GC-CTTC 5aAG-NT-AACC-TTC-GGC-C 5aAG-NT-AACC-TTC-GGGC-C 5aAG-NT-AACC-TTC-GGGC-C 5aAG-NT-AACC-TTC-GGGC-C 5aAGTT-AACC-TTC-GGGC-C 5aAG-NT-AACC-TTC-GGGG
Figure 10	HCV-1 HCV-J HC-J6 HC-J8 PC1_37 PC1_48 BR36	HCV-1 HCV-1 HCV-J HC-J6 HC-J8 HC-J8 HC-J8 HC-J8	(B) HCV - 1 HCV - J HC - J6 HC - J8 PC1 37 BR36

Figure 10 - Continued 7	4891 GTTCAGAATGAAATCACCCTGACGCACCCCAGTCACCAAATACATCATGAAG	4941 ATGCATGTCGGCCGACCTGGAGGTCGTCACGAGCACCTGGGTGCTCGTTG 1b	
Figure	HCV-1 HCV-J HC-J6 HC-J8 PC1_37 PC1_48	HCV-1 HCV-J HC-J6 HC-J8 PC1_37 PC1_48 BR36	HCV-1 HCV-J HC-J6 HC-J8 PC1_37 PC1_48

inued 8	5041 GTCATAGTGGGCAGGGTCGTCTTGTCCGGGAAGCCGGCAATCATACCTGATAA	5091 CAGGGAAGTCCTCTACCGAGAGTTCGATGAAGAGGAGTGCTCTCAGCTGAGTGAGTGAGTCA	5141 ACTTACCGTACATCGAGCAAGGATGATGCTCGCCGAGCAGTTCAAGCAGC-TAAAAAA
- Cont	1a 1b 2a 2b 5a 5a	1a 1b 2a 2b 5a 3a	12 12 23 53 33
Figure 10 - Contin	HCV-1- HCV-J HC-J6 HC-J8 PC1_37 PC1_48 BR36	STATE THE STATE	, HCV - 1 HCV - J HC - J6 HC - J8 PC 1_ 37 PC1_ 48 BR36

Hand Hay I have

5240

5290

tinued 9	5191 AAGGCCCTCGGCCTCCTGCAGACCGCGTCCGTCAGGCAGG	5241 CCCTGCTGTCCAGACCAAAAACTCGAGACCTTCTGGGCGAAGC TC-TGGGTGG-G-GCCTGTA- ACGG-TTCTCCGG-ACAA
.0 - Con	12 12 23 52 53 33	11 32 32 32 32 32 32 32 32 32 32 32 32 32
Figure 10 - Continued	HCV-1 HCV-J HC-J6 HC-J8 PC1_37 PC1_48 BR36	HCV-1 HC-J6 HC-J6 HC-J8 HCV-1 HCV-1 HCV-J HCV-J HCV-J HC-J8 PC1_37 PC1_48 BR36

SEQ ID NO	AETAGARLVVVTV 56	CDELAA
	1286 TTGSPITYSTYGKFLADGGCSGGAYDIIICDECHSTDATSILGIGTVLDQGC	HCV-1 LATATPPGSVTVPHPNIEEVALSTTGEIPFYGKAIPLEVIKGGRHLIFCHSKKKCDELAA HCV-J
	HCV-1 HCV-J HC-J6 HC-J8 PC-1-48	HCV-1 HCV-J HC-J6 HC-J8 PC-1-4

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1406 KLVALGINAVAYYRGLDVSVIPTSGDVVVVATDALMTGYTGDFDSVIDCNTCVTQTVDFSTGL	1466 LDPTFTIETITLPQDAVSRTQRRGRTGRGKPGIYRFVAPGERPSGMFDSSVLCECYDAGC LDPTFTIETITLPQDAVSRTQRRGRTGRGKPGIYRFVAPGERPSGMFDSSVLCECYDAGCT-Q-VSRLY-STAT-Q-VS	1526 AWYELTPAETTVRLRAYMNTPGLPVCQDHLEFWEGVFTGLTHIIDAHFLSQTKQSGENLPY S
HCV-1 HCV-J HC-J6 HC-J8	HCV - 1 HCV - J HC - J6 HC - J8	TUTE SHEET (RULE 26
	565011	TOTAL OFFICE PROPERTY

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330 350 370 370 370 370 370 570	-AVGM-V-HVLTLF-IMIYQAIIMVMIGISH-M-LTLF-LVS-TMLQVIIMIGISH-M-LTLF-LVS-T	FAGVDA ETHVTGGSAGHTVSGFVSLLAPGAKQNVQLINTNGSWHLNSTALG HRVASSTQSLW-SQ-PS-KIVI-R A QTVTA-NARTLTGMFSLR-KII-R V T-YSS-QERA-AG-FTTLYI-RS H-YTT-SRHTQA-AG-FDI-PQ-KLV-SS T-QISSAQ-TY-IA-FITRQ-KLV-S
1a 1b 2a 2h	3a 3b 5a	1a 1b 2a 2b 3a 3b 5a
Figure 12 HCV1 HCVJ HCJ6	<u> </u>	HCV1 HCV1 HCJ6 NZL1 HCJ8 BE95

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* * 025 * * 055	NCNDSLNTGWLAGLFYHHKFNSSGCPERLASCRPLTDFDQGWGPISY AN	HFST-SMSASIEA-RVALQ-ED-	SG-DRITLE-ET-	E-IFIYTQSK-I-F-RLTD		YT	500 510 520	- 1 1	GSGP/DQRPYCWHYPPKPCGIVPAKSVCGPVYCFTPSPVVVGTTDRSGAP	PESS/A-RSQ	VTN-E-MRQV-S-S	VTNDG-MKQ-V-	8		QESK-H-
* *- 430 440	NCNDSLNTGWLAGLFYHHKFNS	S1H	TSB	E-IFIY		\ \ \ \ \	480 490	1	GSGP/DQRPYCWHYPPKPCGIV	PESS/A-R	VTN-E-MRQV-	VTNDG-MR	ITS-DA-RDS		IS-DKRVQE
	6 4	10 2a	2b	3a	3b	5a			1 a	1 b	2a	2b ·	3a	3b	5a
	HCV1	HCJ6	HCJ8	NZL1	HCVTR	BE95			HCV1	HCVJ	HCJ6	HCJ8	NZL1	HCVTR	BE95

Figure 12 · Continued 2

-----E---LL--TRP-QG TYSWGENDIDVFVLNNTRPPL --N--S-V--F-LM----530 1a 1b 2a 2b 3a 3b 5a HCV1 HCVJ HCJ6 HCJ8 NZL1

Figure 13

]	101	/1	11											
0	CGTTGGTAATGGCTCAGCTGCTCCGG			9LV-99-	-CAACC-A-	AACC-A-	AACC-AGGT'-G	AACC-AGGT-G	AACC-AGG'I'-GT'-A	AATC-A-		AAGGT-GI-A-	A			AT(" "A-CAA-CC-CC1CGCCGC11G-1		-TCTTA-CAA-CC-CCI-1GCCGC11G-1	TGTGTAGGGTG-CGTT-AC-	TGTGTAGGGG	CGTGTAGG-AGTG-CG11-GC-	TAGGGGGG	1
	1 a	1a	1a	1 p	1 p	1p	1 p	1 p	1 p	1b	1p	1p	1.b	1b	2a	5p	2a	Sp	3а	3а	3а	3а	5а
SEQ ID																							157
	HCV-1	HCH-H	HC-J1	HCV-J	HCV-BK	HC-J4.83	HC-J4.91											HC-J7	NZL1	HEM26	TH85	US114	BE95
								SI	JBS	TIT	UTE	S	HEE	T (F	RUL	E 2	6)						

	1030 ATCTTGGACATGATCGCTGGTGCTCACTGGGGGACTCCTGGCGGCATAGC
ontinued	1030 11a
Figure 13 - Con	
Figure	HCV - 1 HCH - H HCC - J1 HCV - J HCV - J4 . 93 HC - J4 . 91. HCV - JTA HCV - CHINA HCV - CHINA HCV - CHINA HCV - JK1 HCV - JK1 HCV - JK1 HCV - JK1 HCV - JK1 HCV - JK1 HCC - J6 HCC - J6 HCC - J7 NZL1 NZL1 HEM26 TH85
	SUBSTITUTE SHEET (RULE 26)

	TTTCTCCATGGTGGGGAACTGGGCGAAGGTCCTGGTAGTGCTGCTGC	F E	t	I A I	I'A	i	: 	T W T -	I A I -	A ×	A	- A - T A	AA-T-C-A	- H H H H	I CA - I 1	ני (בּ ביל	īĈ	(A-((CA-CAG-	CA-CGG-	CA-CAG-	(CGCIA-(A-(A-G-1A	V-CGGI-I-
1080	GTATTTCTCCATGGTGGGGAACT	t 1		CC-AT	CC-ATC	CC-AT	CC-ATA	CC-AT	CC-AT	CC-ATGT-	CC-AT	CC-AT	CC-AT	CC-ATC	1	ı	1	1	CACAC	CACACT	CA	CACAC	AC-ATG-ATCCT
	la	la	la	1b	1b	1b	1b	1b	1b	1b	1.b	1 p	15	1 p	2a	2b	2a	2b	3а	3а	3а	3а	5a
	HCV-1	HCH-H	HC-J1	HCV-J	HCV-BK	HC-J4.83	HC-J4.91	HCV-JTA	HCV-JTB	HCV-CHINA	HCV-T	HCV-JK1	HCUNK	HCV-N	HC-J6	HC-J8	HC-J5	HC-J7	NZL1	HEM26	TH85	US114	BE95

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1130 TATTTGCCGGCGTCGACGCGAAACCCACGTCACCGGGGGAAGTGCCGGC
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
HCV-1 HCV-1 HCV-J1 HCV-J2 HCV-BK HCV-BK HC-J4.83 HC-J4.91 HC-J4.91 HC-J4.91 HC-J4.91 HC-J4.91 HC-J4.91 HC-J4.91 HC-J7 HCUNK HCV-CHINA HCUNK HCUNK HC-J5 HC-J5 HC-J5 HC-J5 HC-J5 HC-J5 HC-J5 HC-J5 HC-J5 HC-J5 HC-J5 HC-J5 HC-J7 HC-J5

	CTGATCAACACGGCAGTTGGCACT	1			- A T G	- G T)	ן ן ן				1	5) !		- W-H))V90	V	1) V T 5	
1230	CGTCCAGC	A	1 1 1	AAA-	AA	NA	AA	AA	AA	GA	i I	AAA-	1 1 1 1	AA	AA	T-T		- I.S	VC-G	VC-G	-C-GL	 - - - 	AC-G
	1a	1a	1a	1b	1b	1b	1 p	1b	1 p	1b	1 p	1b	1b	1b	2a	2b	2а	5p	3а	3а	3а	3а	5a
	HCV-1	HCH-H	HC-J1	HCV-J	HCV-BK	HC-J4.83	HC-J4.91	HCV-JTA	HCV-JTB	HCV-CHINA	G HCV-T	HCV-JK1	HCUNK	HCV-N	13 HC-J6	THC-18	20-JH 26)	HC-J7	NZL1	HEM26	TH85	US114	BE95

1280 TGAACTGCAATGATAGCCTCAACACCGGCTGGTTGGCAGGGCTTTTCTAT TGAACTGCAATGATAGCCTCAACACCGGCTGGTTGGCAGGGCTTTTCTAT
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
HCV-1 HCV-1 HCV-31 HCV-31 HCV-34.83 HC-34.91 HC-34.91 HC-34.91 HCV-74.91 HCV-78 HCV-71 HCV-7 HCV-7 HCV-7 HCV-7 HCV-7 HCV-7 HCV-7 HCV-7 HCV-7 HCV-18

Figure 13 - Continued

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inu	1330 CACCACAAGTTCAACTCTTCAGGCTGCTGAGGCTTAGCCAGCTGCCG CACCACAAGTTCAACTCTTCAGGCTGTCTTCAAGCCTAGCCAGCTGCCG CACCACACTCTTCAACTCTTCAGGCTGTCTTCAACTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT
- Cont	10 11 11 11 11 11 11 12 13 13 13 13 13 13 13 13 13
Figure 13	HCV-1 HCH-H HC-J1 HCV-J HCV-BK HCV-J4.83 HC-J4.91 HCV-JTB HCV-JTB HCV-JTB HCV-JTB HCV-JTB HCV-JTB HCV-JTB HCV-JTB HCV-JK HCV-J

	CGAGAA CAAA
ontinued 8	1380 ACCCCTTACCGATTTTGACCAGGGCTGGGGCCCTATCAGTTAN -G
Ŭ	
Figure 13 - Continued	HCV-1 HCH-H HC-J1 HCV-BK HCV-J4.91 HC-J4.91 HC-J4.91 HCV-JTA HCV-JTB HCC-JTB HCC-JT

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	430 CGGAAGCGGCCCC GACCAGCGCCCCTACTGCTGGCACTACCCCCAA CGGAAGCGGCCCC
6 panu	1430 ACGGAAGCGCCCC ACGGAAGCGCCCC
Conti	1a 11a 11b 11b 11b 12a 12a 12a 13a 3a 3a
Figure 13 - Conti	HCV-1 HCH-H HCV-JJ HCV-JJ HCV-J4.83 HC-J4.91 HCV-JTB HCV-JTB HCV-CHINA HCV-CHINA HCV-T HCV-J6 HCV-J6 HCV-J6 HCV-J6 HCV-J6 HCV-J7 HCV-J7 HCV-J7 HCV-J8 HCV-J8

Continued

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-G-T---T-A--CC--C--G--ATCA-----C CGG--G-----NG-G------N--CC-NGAG--C -G----TACCG----C--ATCA----C J--9J---T--B-LJ--J--J--------G----T-AC----C--G--ATCA-----C -G----TAAA-G---C--A--ATCA-----C T--9D--9-L--9--D--D--D-------------G--T--C--A--C-----G-TC----G--AG--T---G-A--CT-----GCTC---CGG--G--T----C--A-----TC-CAG---C----G--T-----C-----TT-CAG---C----G--T-------A--TT-CAG---CG-AAG----C--C--A--T---TC-GAG---CGG-AG--T----C--A--T---TC-CAG---CGG-AG--T----C--A----TC-CAG---CC--AA--TACC--C--A--T---TC-GAG---C---AG--T----CA-A---CG-TCCGAG-C AAACCTTGCGGTATTGTGCCCGCGAAGAGTGTG CG---G----G--C----T---TC-CAG----G----T---C------CG---G--T----C--A-----TC-CAG--CG---G--T----C--A-----TC-CAG--11b 11b 22a 22b 22b 22b 33a 15 15 15 15 15 15 1p la HCV-CHINA HC-J4.91 HC-J4.83 HCV-JTB HCV-JTA HCV-JK1 US114 HEM26 HC-J5 HC-J7 Figure HC-J8 HCV-BK HCV-T HC-J6 HCV-N TH85 NZL1 HCUNK HCV-J HCH-H HC-J1 HCV-1 SUBSTITUTE SHEET (RULE 26)

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RULE 53 (37 C.F.R. 1.53) DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
As a below named inventor 1 hereby declare that my residence post office address and ottobership are as stated below next to my name, and 1

C JS GENOTYPE	S AND THEIR USE	for which a patent is sought on the AS THERAPEUTIC AND	e invention entitled: " DIAGNOSTIC ACF	'NEW SEQUENCES OF HEPATIT
the specification of which (check applicable boxts))	TO NOL	
is attached hereto				
was filed on		as U.S. Application Senal No.		(Atty Okt. No.
		PCT EP94/01323	on 27 A	PRIL 1994
ain d (if applicable to U.S	•			
amendment reterred to about the second of th	ove. I acknowledge the loy claim foreign phonty identified below any for or, if no phonty is claim	duty to disclose information which benefits under 05 U.S.C. 119/365	is material to the pater of any roreign applicat ntor's certificate naving	ing the claims, as amended by any intability of this application in accordance con(s) for patent or inventor's certificate a filing date before that of the application
As plication Number		Country		Davida 26
93.401 099.2		EUROPE		Däy/Month/Year Filed 27 APRIL: 1993
93.402.019.9		EUROPE		<u> </u>
93.402.019.9		LUXUFL		05 AUGUST 1993
Application Senal No. PCT/EP94/01323		Day/Month/Year File		pending, abandoned
to be due, and further that or imprisonment, or both, c	these statements were inder Section 1001 of T	made with the knowledge that will the 18 of the United States Code a	ifui faise statements and and that such willful fals	d the like so made are punishable by fini se statements may eodardize the validity
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FOR ADDITIONAL INVENTORS, check box 📋 and attach sheet with same information and signature and date for each.

SEQUENCE LISTING

- (1) GENERAL INFORMATION:
 - (i) APPLICANT:
 - (A) NAME: Innogenetics sa.
 - (B) STREET: Industriepark Zwijnaarde 7, box 4
 - (C) CITY: Ghent
 - (E) COUNTRY: Belgium
 - (F) POSTAL CODE (ZIP): B-9052
 - (G) TELEPHONE: 00 32 9 241 07 11
 - (H) TELEFAX: 00 32 9 241 07 99
 - (11) TITLE OF INVENTION: New sequences of hepatitis C virus genotypes for diagnosis, prophylaxis and therapy.
 - (iii) NUMBER OF SEQUENCES: 270
 - (iv) COMPUTER READABLE FORM.
 - (A) MEDIUM TYPE: Floppy disk
 - (B) COMPUTER: IBM PC compatible
 - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
 - (D) SCFTWARE: PatentIn Release #1.0, Version #1.25 (EPO)
 - (2) INFORMATION FOR SEQ ID NO: 1:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 213 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (i1) MOLECULE TYPE: cDNA
 - (111) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: BR34-4-20
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..213
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

CTC ACG GAA CGG CTT TAC TGC GGG GGC CCT ATG TTC AAC AGC AAG GGG Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly 10 5

GCC CAG TGT GGT TAT CGC CGC TGC CGT GCC AGT GGA GTT CTG CCT ACC Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr

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AGC TTC GGC AAC ACA ATC ACT TGC TAC ATC AAG GCC ACA GCG GCT GCA 144 Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala 35 4.0

AGG GCC GCA GGC CTC CGG AAC CCG GAC TTT CTT GTC TGC GGA GAT GAT 192 Arg Ala Ala Gly Leu Arg Asn Pro Asp Phe Leu Val Cys Gly Asp Asp 50 55

CTG GTC GTG GTG GCT GAG AGT 213 Leu Val Val Val Ala Glu Ser 65

(2) INFORMATION FOR SEQ ID NO: 2:

20

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 71 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (11) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly

Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr 20 25

Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala 40

Arg Ala Ala Gly Leu Arg Asn Pro Asp Pne Leu Val Cys Gly Asp Asp 60 50 5.5

Leu Val Val Val Ala Glu Ser

- (2) INFORMATION FOR SEQ ID NO: 3:
 - (1) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 213 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (11) MOLECULE TYPE: cDNA
 - (V11) IMMEDIATE SOURCE:

(B) CLONE: BR36-23-18

- (1x) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..213

	(x1)	SEC	OUEN	TE DE	ESCRI	PTIC	ON: 5	EQ I	D NO): 3:						
					TAC Tyr											48
					Arg											96
					ATC Ile											144
					CGG Arg										GAT Asp	192 -
					GAG Glu 70											213
	(ii)	() () () () ()	A) L B) T D) T LECU	ENGT YPE: OPOL LE T	CHAI H: 7: ami: OGY: YPE:	l am no a lin pro	ino cid ear cein	acid	s	O: 4	:					
Leu 1	Thr	Glu	Arg	Leu 5		Cys	Gly	Gly	Pro		Phe	: Asn	Ser	Lys 15	Gly	
Ala	Gln	Cys	Gly 20	-	Arg	Arg	Cys	Arg 25		Ser	Gly	Val	Leu 30		Thr	
Ser	Phe	Gly 35		Thr	·Ile	Thr	Cys 40	-	Ile	. Lys	Ala	Thr 43		a Ala	Ala	
Arg	Ala 50		Gly	r Leu	Arg	Asr 59		Asp	Phe	e Leu	(Va)	-	Gly	/ As <u>r</u>	qaA c	
Leu 65		Val	. Val	. Ala	Glu 70		:									
(2)	INF	ORM	TION	1 FOF	R SEC) ID	: CM	5:								
	(1	,	(A) I (B) 5 (C) 5	LENGT TYPE STRAL	THARA TH: 2 : nuc NDEDM	213 l Cleic VESS	pase = ac: : S1	pai: id	rs							

	(ii)	MOI	ECUL	E TY	PE:	CDNA										
(iii)	HYE	отне	TICA	L: N	Ю										
(iii)	ANT	I-SE	NSE :	NO											
(viı)		ŒDIA 3) CI				-18									
	(ix)	(P	TURE L) NA B) LO	WE\R			!13									
	(xi)	SEÇ	OUENC	E DE	ESCRI	PTIC	N: 5	EQ I	ED NO): 5:						-
														AAG Lys 15		48
														CCT		96
														GCC Ala		144
														GAT Asp		192
			GTG Val													213
(2)	INF	ORMA'	rion	FOR	SEQ	ID 1	NO :	6 <i>:</i>								
		()	SEQUI A) L B) T	ENGT: YPE :	H: 7	l am no a	ino cid									
	(li) MO	LECU	LE T	YPE:	pro	tein									
	(xi) SE	QUEN	CE D	ESCR	IPTI	ON:	SEQ	ID N	10: 6	:					
Leu 1	Thr	Glu	Arg	Leu 5		Cys	Gly	Gly	Pro 10		Phe	: Asn	. Ser	Lys 15	Gly	
Ala	Gln	Cys	Gly 20	-	Arg	Arg	Cys	Arg		se:	: Gly	v Val	. Leu 30		Thr	
Ser	Phe	Gly 35		Thr	Ile	Thr	Cys 40		: Ile	e Lys	Ala	Thr 45		Ala	Ala	

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99

Lys Ala Ala Gly Leu Arg Ser Pro Asp Phe Leu Val Cys Gly Asp Asp 55

Leu Val Val Val Ala Glu Ser

- (2) INFORMATION FOR SEQ ID NO: 7:
 - (1) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 213 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (11) MCLECULE TYPE: cDNA
 - (111) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: BR36-23-20
 - (1x) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..213
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:
- CTC ACG GAG CGG CTT TAC TGC GGG GGC CCT ATG TTT AAC AGC AAA GGG Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly 1
- GCC CAG TGT GGT TAT CGC CGT TGC CGT GCC AGT GGA GTT CTG CCT ACC Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr
- AGC TTC GGC AAC ACA ATC ACT TGT TAC ATC AAA GCC ACA GCG GCC GCA Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala
- AAA GCC GCA GGC CTC CGG AGC CCG GAC TTT CTT GTC TGC GGA GAT GAT Lys Ala Ala Gly Leu Arg Ser Pro Asp Phe Leu Val Cys Gly Asp Asp

CTG GTC GTG GTG GCT GAG AGT 213 Leu Val Val Val Ala Glu Ser 65 70

- (2) INFORMATION FOR SEQ ID NO: B:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 71 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: protein	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:	
Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly 1 5 10 15	
Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr 20 25 30	
Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala 35 40 45	
Lys Ala Ala Gly Leu Arg Ser Pro Asp Phe Leu Val Cys Gly Asp Asp 50 55 60	
Leu Val Val Val Ala Glu Ser 65 70	
(2) INFORMATION FOR SEQ ID NC: 9.	
(1) SEQUENCE CHARACTERISTICS: (A) LENGTH: 213 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: cDNA	
(ili) HYPOTHETICAL: NO	
(i1i) ANTI-SENSE: NO	
(vii) IMMEDIATE SOURCE: (B) CLONE: BR33-2-17	
(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 1213	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:	
CTC ACG GAG CGG CTT TAC TGC GGG GGC CCT ATG TTC AAC AGC AAG GGG Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly 1 5 10 15	48
GCC CAG TGT GGT TAT CGC CGT TGT CGT GCC AGT GGA GTT CTG CCT ACC Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr 20 25 30	96
AGT TTC GGC AAC ACA ATC ACT TGT TAC ATC AAG GCC ACA GCG GCT GCA Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala 35 40 45	144

AAA GCC GCA GGC CTC CGG AAC CCG GAC TTT CTT GTT TGC GGA GAT GAT 192

Lys Ala Ala Gly Leu Arg Asn Pro Asp Phe Leu Val Cys Gly Asp Asp 50 60

TTG GTC GTG GTG GCT GAG AGT Leu Val Val Val Ala Glu Ser 213

- (2) INFORMATION FOR SEQ ID NO: 10:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 71 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (11) MOLECULE TYPE: protein
 - (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly
1 10 15

Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr 20 25 30

Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala 40 45

Lys Ala Ala Gly Leu Arg Asn Pro Asp Phe Leu Val Cys Gly Asp Asp 50 60

Leu Val Val Val Ala Glu Ser 65 70

- (2) INFORMATION FOR SEQ ID NO: 11:
 - (1) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 213 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: BR33-2-21
 - (1x) FEATURE:
 - (A) NAME/KEY: CDS -
 - (B) LOCATION: 1..213
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

SUBSTITUTE SHEET (RULE 26)

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						 AGC Ser			48
			Cys	Ala		 CTG Leu 3J			96
						 GCG Ala	 GCA Ala	1	44
	 	 				 GGA Gly		1	.92

- (2) INFORMATION FOR SEQ ID NO: 12:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 71 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly
1 5 10 15

Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr 20 25 30

Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala 35 40 45

Lys Ala Ala Gly Leu Arg Asn Pro Asp Phe Leu Val Cys Gly Asp Asp 50 55 60

Leu Val Val Val Ala Glu Ser 65 70

- (2) INFORMATION FOR SEQ ID NO: 13:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 541 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (111) HYPOTHETICAL: NO

(iii)	ANTI-	SENSE	: NO
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(vii) IMMEDIATE SOURCE:
(B) CLONE: HD10-2-5

(ix) FEATURE:

(A) NAME/KEY: CDS
(B) LOCATION: 2..541

(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

C GTC GGC GCT CCT GTA GGA GGC GTC GCA AGA GCC CTT GCG CAT GGC Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly 1 5 10 15													
GTG AGG GCC CTT GAA GAC GGG ATA AAT TTC GCA ACA GGG AAT TTG CCC Val Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro 20 25 30	- 94												
GGT TGC TCC TTT TCT ATC TTC CTT CTT GCT CTG TTC TCT TGC TTA ATC Gly Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile 35 40 45	142												
CAT CCA GCA GCT AGT CTA GAG TGG CGG AAC ACG TCT GGC CTC TAT GTC His Pro Ala Ala Ser Leu Glu Trp Arg Asm Thr Ser Gly Leu Tyr Val 50 55 60	190												
CTT ACC AAC GAC TGT TCC AAT AGC AGT ATT GTG TAT GAG GCC GAT GAC Leu Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp 65 70 75	238												
GTT ATT CTG CAC ACA CCC GGC TGT GTA CCT TGT GTT CAG GAC GGT AAT Val Ile Leu His Thr Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn 80 85 90 95	296												
ACA TOT GCG TGC TGG ACC CCA GTG ACA CCT ACA GTG GCA GTC AGG TAC Thr Ser Ala Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr 100 105 110	334												
GTC GGA GCA ACC ACC GCT TCG ATA CGC AGG CAT GTA GAC ATG TTG GTG Val Gly Ala Thr Thr Ala Ser Ile Arg Arg His Val Asp Met Leu Val 115 120 125	382												
GGC GCG GCC ACG ATG TGC TCT GCT CTC TAC GTG GGT GAT ATG TGT GGG Gly Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys.Gly 130 135 140	430												
GCC GTC TTC CTC GTG GGA CAA GCC TTC ACG TTC AGA CCT CGT CGC CAT Ala Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg Arg His 145 150 155	478												
CAA ACG GTC CAG ACC TGT AAC TGC TCA CTG TAC CCA GGC CAT CTT TCA Gln Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser 160 165 170 175	526												

GGA CAC CGA ATG GCT Gly His Arg Met Ala 180

541

- (2) INFORMATION FOR SEQ ID NO: 14:
 - (i) SEQUENCE CHARACTERISTICS.
 - (A) LENGTH: 180 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (11) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val

Arg Ala Leu Glu Asp Gly Ile Asm Phe Ala Thr Gly Asm Leu Pro Gly 20 25 30

Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile His
35 40 45

Pro Ala Ala Ser Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu 50 55 60

Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val
65 70 75 80
Lie Leu His Thr Pro Gly Cys Val Pro Cyr Val Gle Asp Si

Ile Leu His Thr Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn Thr 85 90 95

Ser Ala Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr Val

Gly Ala Thr Thr Ala Ser Ile Arg Arg His Val Asp Met Leu Val Gly 115 120 125

Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys Gly Ala 130 140

Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg Arg His Gln 145 150 155 160

Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser Gly 165 170 175

His Arg Met Ala 180

- (2) INFORMATION FOR SEQ ID NO: 15:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 541 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(i1) MOLECULE TYPE: CDNA	
(111) HYPOTHETICAL: NO	
(111) ANTI-SENSE: NO	
(V1i) IMMEDIATE SOURCE: (B) CLONE: HD10-2-14	
(1x) FEATURE: (A) NAME/KEY: CDS (B) LCCATION: 2541	
(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 15:	
C GTC GGC GCT CCT GTA GGA GGC GTC GCA AGA GCT CTT GCG CAT GGC Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly 1 5 10	- 46
GTG AGG GCC CTT GAA GAC GGG ATA AAT TTC GCA ACA GGG AAT TTG CCC Val Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro 20 25 30	94
GGT TGC TCC TTT TCT ATC TTC CTT CCT GCT CTG TTC TCT TGC TTA ATC Gly Cys Ser Phe Ser Ile Phe Leu Pro Ala Leu Phe Ser Cys Leu Ile 35 40 45	142
CAT CCA GCA GCT AGT CTA GAG TGG CGG AAC ACG TCT GGC CTC TAT GTC His Pro Ala Ala Ser Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val 50 55 60	190
CTT ACC AAC GAC TGT TCC AAT AGC AGT ATT GTG TAT GAG GCC GAT GAC Leu Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp 65 70 75	233
GTT ATT CTG CAC ACA CCC GGC TGT GTA CCT TGT GTT CAG GAC GGT AAT Val Ile Leu His Thr Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn 80 85 90 95	286
ACA TCT GCG TGC TGG ACC CCA GTG ACA CCT ACA GTG GCA GTC AGG TAC Thr Ser Ala Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr 100 105 110	33≟
GTC GGA GCA ACC ACC GCT TCG ATA CGC AGG CAT GTA GAC ATA TTG GTG Val Gly Ala Thr Thr Ala Ser Ile Arg Arg His Val Asp Ile Leu Val 115 120 125	3 5 2
GGC GCG GCC ACA ATG TGC TCT GCT CTC TAC GTG GGT GAT ATG TGT GGG Gly Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys Gly 130 135 140	430
GCC GTC TTC CTC GTG GGA CAA GCC TTC ACG TTC AGA CCT CGT CGC CAT Ala Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg Arg His 145 150 155	47

CAA ACG GTC CAG ACC TGT AAC TGC TCA CTG TAC CCA GGC CAT CTT TCA

Gln Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser 160 165 170 170

GGA CAC CGA ATG GCT Gly His Arg Met Ala 180

541

- (2) INFORMATION FOR SEQ ID NO: 16:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 190 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (11) MOLECULE TYPE: protein
 - (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val

Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro Gly 20 25 30

Cys Ser Phe Ser Ile Phe Leu Pro Ala Leu Phe Ser Cys Leu Ile His

Pro Ala Ala Ser Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu 50 55 60

Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val 65 70 75 80

Ile Leu His Thr Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn Thr 85 90 95

Ser Ala Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr Val

Gly Ala Thr Thr Ala Ser Ile Arg Arg His Val Asp Ile Leu Val Gly
115 120 125

Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys Gly Ala 130 135 140

Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg Arg His Gln 145 150 150 155

Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser Gly
165 170 175

His Arg Met Ala 180

- (2) INFORMATION FOR SEQ ID NO: 17 :
 - (1) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 541 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(i1) MOLECULE TYPE: cDNA	
(lil) HYPCTHETICAL: NO	
(iii) ANTI-SENSE: NO	
(V11) IMMEDIATE SOURCE: (B) CLONE: HD10-2-21	
(1x) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 2541	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:	
C GTC GGC GCT CCT GTA GGA GGC GTC GCA AGA GCC CTT GCG CAT GGC Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly 1 5 10	46
GTG AGG GCC CTT GAA GAC GGG ATA AAT TTC GCA ACA GGG AAT TTG CCC Val Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro 20 25 30	94
GGT TGC TCC TTT TCT ATC TTC CTT CTT GCT CTG TTC TCT TGC TTA ATC Gly Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile 35 40 45	142
CAT CCA GCA GCT AGT CTA GAG TGG CGG AAC ACG TCT GGC CTC TAC GTC His Pro Ala Ala Ser Leu Glu Trp Arg Asm Thr Ser Gly Leu Tyr Val 50 55 60	190
CTT ACC AAC GAC TGT TCC AAT AGC AGT ATT GTG TAT GAG GCC GAT GAC Leu Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp 65 70 75	238
GTT ATT CTG CAC ACA CCC GGC TGT GTA CCT TGT GTT CAG GAC GGT AAT Val Ile Leu His Thr Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn 80 85 90 95	286
ACA TCT GCG TGC TGG ACC CCA GTG ACA CCT ACA GTG GCA GTC AGG TAC Thr Ser Ala Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr 100 105 110	334
GTC GGA GCA ACC ACC GCT TCG ATA CGC AGG CAT GTA GAC ATA TTG GTG Val Gly Ala Thr Thr Ala Ser Ile Arg Arg His Val Asp Ile Leu Val 115 120 125	382
GGC GCG GCC ACG ATG TGC TCT GCT CTC TAC GTG GGT GAT ATG TGT GGG Gly Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys Gly	430

130

140

GCC Ala	GTC Val 145	TTC Phe	CTC Leu	GTG Val	GGA Gly	CAA Gln 150	GCC Ala	TTC Phe	ACG Thr	TTC Phe	AGA Arg 155	CCT Pro	CGT Arg	CGC Arg	CAT H1s	478
														CTT Leu		526
GGA Gly	CAC His															541

(2) INFORMATION FOR SEO ID NO: 18:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 180 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (11) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18.

Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val 1

Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro Gly 20 25 30

Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile His

Pro Ala Ala Ser Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu 50 60

Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val
65 70 75

Ile Leu His Thr Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn Thr 85 90 95

Ser Ala Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr Val 100 105 110

Gly Ala Thr Thr Ala Ser Ile Arg Arg His Val Asp Ile Leu Val Gly
115 120 125

Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys Gly Ala 130 135 140

Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg Arg His Gln 145 150 155 160

Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser Gly
165 170 175

His Arg Met Ala

(2)	INFO	RMAT	ON E	FOR S	EQ 1	D NO): 19) :								
	(i)	(B)	JENCE LEX TYI STI	NGTH PE: I RAND	: 541 nucle EDNES	L bas eic a ES: s	se pa acid singl	airs								
	(ii)	MOL	ECUL	E TY	?E: (EDNA										
(iıı)	HYP	OTHE	rical	L: NO											
(iii)	ANT	I-SE	NSE.	МО											
(VII)	IMM (B	EDIA				13									-
	(1x)	_	TURE) NAI) LO	ME/K			41									
	(x1)	SEÇ	UENC	E DE	SCRI	PTIC	N: S	EQ I	⊃ NC	: 19	:					
Va				o Va						g Al			G CA' a Hi	s Gl		4.5
													AAT Asn			94
													TGC Cys 45			142
													CTC Leu			190
													GCC Ala			238
													GAC Asp			286
													GTC Val		Tyr	334
GTC	GGA	GCA	ACC	ACC	GCT	TCG	ATA	- . CGC	AGT	CAT	GTG	GAC	CTA	TTA	GTG	382

Val Gly Ala Thr Thr Ala Ser Ile Arg Ser His Val Asp Leu Leu Val 115 120 125

			TGC Cys				 		4 30
		-	GGA Gly				 		478
			TGT Cys 165				 		525
GGA Gly	 	ATG Met							541

110

(2) INFORMATION FOR SEQ ID NO: 20:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 180 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

(11) MOLECULE TYPE: protein

(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val

1 5 10 15

Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro Gly

Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile His $35 \hspace{1cm} 40 \hspace{1cm} 45 \hspace{1cm}$

Pro Ala Ala Ser Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu 50 55 60

Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val 65 70 75 80

Ile Leu His Thr Pro Gly Cys Ile Pro Cys Val Gln Asp Gly Asn Thr 85 90 95

Ser Thr Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Lys Tyr Val

Gly Ala Thr Thr Ala Ser Ile Arg Ser His Val Asp Leu Leu Val Gly
115 120 125

Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys Gly Ala 130 135 140

Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg Arg His Gln 145 150 150

Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser Gly

165 170 175

His Arg Met Ala 180

- (2) INFORMATION FOR SEQ ID NO: 21:
 - (1) SEQUENCE CHAPACTERISTICS:
 - (A) LENGTH: 541 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (ill) HYPOTHETICAL: NO
 - (111) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: BR36-9-20
 - (1x) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 2..541
 - (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

С	GTC	GGC	GCT	CCC	GTA	GGA	GGC	GTC	GCA	AGA	GCC	CTT	GCG	CAT	GGC	46
	Val	Gly	Ala	Pro	Val	Gly	Gly	Val	Ala	Arg	λla	Leu	Ala	His	Gly	
	1				5					10					15	

GTG	AGG	GCC	CTT	GAA	GAC	GGG	ATA	AAT	TTC	GCA	ACA	GGG	AAT	TTG	CCC	94
Val	Arg	Ala	Leu	Glu	Asp	Gly	Ile	Asn	Phe	Ala	Thr	Gly	Asn	Leu	Pro	
				2.0					25					30		

GGT	TGC	TCC	TTT	TCT	ATT	TTC	CTT	CTT	GCT	CTG	TTC	TCT	TGC	TTA	ATT	142
Gly	Cys	Ser	Phe	Ser	Ile	Phe	Leu	Leu	Ala	Leu	Phe	Ser	Cys	Leu	Ile	
			35					40					45			

CAT	CCA	GCA	GCT	AGT	CTA	GAG	TGG	CGG	AAT	ACG	TCT	GGC	CTC	TAT	GTC	190
His																
		E 0					= =					60				

CTT	ACC	AAC	GAC	TGT	TCC	AAT	AGC	AGT	ATT	GTG	TAC	GAG	GCC	GAT	GAC	238
															Asp	
	65					70					75					

GTT Val													
vai	TIE	пел	1172	1117	FIG	Gry	CyJ	110	 C, 3	-	 	 -	
80					85				90			95	

ACA	TCC	ACG	TGC	TGG	ACC	CCA	GTG	ACA	CCT	ACA	GTG	GCA	GTC	AAG	TAC	334
Thr	Ser	Thr	Cys	Trp	Thr	Pro	Val	Thr	Pro	Thr	Val	Ala	Val	Lys	Tyr	
				100					105					110		

									112								
														TTA Leu			382
													• • • •	TGT Cys			430
														CGC Arg	CAT His		478
														CTT	TCA Ser 175		526
			ATG Met													-	541
(2)	INF	ORMA	TION	FOR	SEQ	ו כו	NO :	22:									
(1) SEQUENCE CHARACTERISTICS:(A) LENGTH: 180 amino acids(B) TYPE: amino acid(D) TOPOLOGY: linear																	
	(ii) MOLECULE TYPE: protein																
	/	٠	~~~ ~	n			ONT :	c=0	1	· .	٦.						

(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val 1 10 15

Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro Gly 20 25 30

Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile His 35 40 45

Pro Ala Ala Ser Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu 50 60

Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val 65 70 75

Ile Leu His Thr Pro Gly Cys Ile Pro Cys Val Gln Asp Gly Asn Thr \$85\$

Ser Thr Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Lys Tyr Val

Gly Ala Thr Thr Ala Ser Ile Arg Ser His Val Asp Leu Leu Val Gly 115 $\,$ 125

Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys Gly Ala 130 140

Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg Arg His Gln 145 150 155 160	
Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser Gly 165 170 175	
His Arg Met Ala 180	
(2) INFORMATION FOR SEQ ID NG: 23:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 541 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(11) MOLECULE TYPE: cDNA	
(iii) HYPOTHETICAL: NC	
(111) ANTI-SENSE: NC	
(vii) IMMEDIATE SOURCE. (B) CLONE: BR33-1-10	
<pre>(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 2541 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:</pre>	
C GTC GGC GCT CCC GTA GGA GGC GTC GCA AGA GCC CTT GCG CAT GGC Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly 1 5 10	46
GTG AGG GCC CTT GAG GAC GGG ATA AAC TTC GCA ACA GGG AAT TTG CCC Val Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro 20 25 30	94
GGT TGC TCC TTT TCT ATC TTC CTT CTT GCT CTG TTC TCT TGC TTA ATC Gly Cys Ser Phe Ser Ile Pne Leu Leu Ala Leu Phe Ser Cys Leu Ile 35 40 45	142
CAT CCA GCA GCT GGT CTA GAG TGG CGG AAT ACG TCT GGC CTC TAT GTC	190
His Pro Ala Ala Gly Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val 50 55 60	
CTT ACC AAC GAC TGT TCC AAT AGT AGT ATT GTG TAT GAG GCC GAT GAC Leu Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp 65 70 75	238
GTT ATT CTG CAC GCG CCC GGC TGT GTA CCT TGT GTC CAG GAC GGC AAT	

ACG T									334
GTC G						 	-		382
GGC G									430
GCC G Ala V									478
CAA A Glm I 160								TCA Ser 175	525
GGA C Gly H									541

(2) INFORMATION FOR SEQ ID NO: 24:

- (1) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 180 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:

Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val 1 5 10 15

Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro Gly \$20\$

Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile His
35 40 45

Pro Ala Ala Gly Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu 50 60

Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val 65 70 75 80

Ile Leu His Ala Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn Thr

Ser Thr Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr Val

Gly Ala Thr Thr Ala Ser Ile Arg Ser His Val Asp Leu Leu Val Gly

	115				120					143					
Ala Ala 130	Thr Me	c Cys	Ser	Ala 1 135	Leu 7	ryr V	/al (Gly	Asp 140	Met	Cys	Gly	Ala	ı	
Val Phe	Leu Va	al Gly	Gln 150	Ala	Phe 1	Thr !	Phe	Arg 155	Pro	Arg	Arg	His	Gl:	n D	
Thr Val	Gla Ti	ır Cys 165		Cys	Ser :	Leu 1	Tyr 170	Pro	Gly	His	Leu	Ser 175	Gl	?	
His Arg	1	80	SEQ	ID N	10: 2	5 :									
(i)	(B) (C)	ENCE C LENGI TYPE STRAI TOPOI	TH: 5 : nuc NDEDN	41 ba leic ESS:	se p acid sing	airs								-	
) MOLE				Ā										
) HYPC														
(111) ANTI	-SENS	=. NC	,											
(vii) IMME (B)	EDIATE CLON			-19										
(ix		TURE:) NAME) LOCA													*
(x:	ı) SEQ	UENCE	DESC	RIPTI	ON:	SEQ	ID N	10 :	25:						
C GTC C Val C	GGC GC Gly Al	T CCC a Pro	GTA Val 5	GGA (GC G	TC G	CA A	AGA Arg 10	GCC Ala	CTT	GCG Ala	CAT His	GGC Gly 13	<i>'</i>	46
GTG AG Val Ar	g GCC g Ala	Leu G	AG GA lu As 20	c GGG	g ATA y Ile	A AAC a Asi	TTO n Pho 2	e A	CA A	CA G(hr G)	eg Al Ly Ai	211 114	rg (eu 1 30	CCC Pro	94
GGT TG Gly Cy	C TCT s Ser	TTT T Phe S	CT AT	TC TT Le Ph	C CT e Le	T CT u Le 4	u Al	T C'	IG T eu P	TC T he S	er C	GC T ys L 45	TA . eu	ATC Ile	142
CAT CO	IA GCA co Ala 50	GCT C	GT C	TA GA eu Gl	u Tr	G CG P Ar	G AA	AT A sn T	CG Thr S	er G	GC C	TC T eu T	'AT 'Yr	GTC Val	19
Leu T	CC AAC nr Asn	GAC 1	IGT T Cys S	er As	AT AG sn Se	T AC	T AT	IT G le V	TG : /al '	TAT C TYT C 75	AG C	CC C	TAE Asp	GAC Asp	23

GTT Val	ATT Ile	CTG Leu	CAC H1s	GCG Ala	CCC Pro	GGC Gly	TGT Cys	GTA Val	CCT Pro	TGT Cys	GTC Val	CAG Gln	GAC Asp	GGC Glv	AAT Asn	286
80					85					90					95	
ACG Thr	TCT Ser	ACA Thr	TGC Cys	TGG Trp	ACC Thr	CCA Pro	GTA Val	ACA Thr	CCT Pro	ACA Thr	GTG Val	GCA Ala	GTC Val	AGG Arg	TAC Tvr	334
				100					105					110	-2-	
GTC Val	GGG G1 v	GCA	ACC	ACC Thr	GCT	TCG	ATA	CGC	AGT	CAT	GTG	GAC	CTG	TTA	GTA	382
	U1;	n_u	115		n_a	JC.	1.3	120	Jei	#12	vai	ASD	125	Leu	Val	
GGC	GCG	GCC	ACG	ATG	TGC	TCT	GCG	CTT	TAC	GTG	GGT	GAT	ATG	TGT	GGG	430
GTA	WIG	130	inr	Met	Cys	ser	135	Leu	TYT	Val	Gly	Asp 140	Met	Cys	Gly	
GCC	GTC	TTC	CTC	GTG	GGA	CAA	GCC	TTC	ACG	TTC	AGA	CCC	CGC	CGC	CAT	478
ALG	145	rne	Leu	Val	GTA	150	Ala	Pne	Thr	Phe	Arg 155	Pro	Arg	Arg	His -	
				ACC												526
150	inr	vai	GIN	Thr	165	AST	Cys	Ser	Leu	170	Pro	Gly	His	Leu	Ser 175	
GGA	CAT	CGA	ATG	GCT												541
Gly	Hıs	Arg	Met	Ala 180												34

(2) INFORMATION FOR SEQ ID NO: 26:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 180 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:

Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val

1 10 15

Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro Gly

Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile His $35 \hspace{1cm} 40 \hspace{1cm} 45 \hspace{1cm} .$

Pro Ala Ala Gly Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu 50 55 60

Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val 65 70 75 80

Ile Leu His Ala Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn Thr 85 90 95

117	
Ser Thr Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr Val	
Gly Ala Thr Thr Ala Ser Ile Arg Ser His Val Asp Leu Leu Val Gly 115 120 125	
Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys Gly Ala 130 135 140	
Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg Arg His Gln 145 150 155 160	
Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser Gly 165 170 175	
His Arg Met Ala 180	
(2) INFORMATION FCR SEQ ID NO: 27:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 541 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(11) MOLECULE TYPE: cDNA	
(iii) HYPOTHETICAL: NO	
(iii) ANTI-SENSE: NO	
<pre>(vii) IMMEDIATE SOURCE:</pre>	
C GTC GGC GCT CCC GTA GGA GGC GTC GCA AGA GCC CTT GCG CAT GGC Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly 1 5 10 15	46
GTG AGG GCC CTT GAG GAC GGG ATA AAC TTC GCA ACA GGG AAT TTG CCC Val Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro	94
GGT TGC TCT TTT TCT ATC TTC CTT CTT GCT CTG TTC TCT TGC TTA ATC Gly Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile 35 40 45	142
CAT CCA GCA GCT GGT CTA GAG TGG CGG AAT ACG TCT GGC CTC TAT GTC	190

His Pro Ala Ala Gly Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val

60

55

50

-		TGT Cys								238
		GCG Ala								286
		TGG Trp 100								334
		ACC Thr								382
 	 	ATG Met	 						-	430
		GTG Val								478
		ACC Thr				Pro		TCA Ser 175		526
	ATG Met									541

(2) INFORMATION FOR SEQ ID NO: 28:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 180 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val

1 5 10 15

Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro Gly

20 25 30

Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile His 35 40 45

Pro Ala Ala Gly Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu 50 55 60

Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val 65 70 75 80

Ile	Leu	His	Ala	85 28	Gly	Cys	Val	Pro	Суs 90	Val	Gln	Asp	Gly	Asn 95	Thr	
Ser	Thr	Cys	Trp 100	Thr	Pro	Val	Thr	Pro 105	Thr	Val	Ala	Val	Arg 110	Tyr	Val	
Gly	Ala	Thr 115	Thr	Ala	Ser	Ile	Arg 120	Ser	His	Val	qzA	Leu 125	Leu	Val	Gly	
Ala	Ala 130	Thr	Met	Cys	Ser	Ala 135	Leu	Tyr	Val	Gly	Asp 140	Met	Cys	Gly	Ala	
Val 145	Phe	Leu	Val	Gly	Gln 150	Aia	Phe	Thr	Phe	Arg 155	Pro	Arg	Arg	Hıs	Gln 160	
Thr	Val	Gln	Thr	Cys 163	Asn	Cys	Ser	Leu	Тут 170	Pro	Gly	His	Leu	Ser 175	Gly	
His	Arg	Met	Ala 180													-
(2)	INF	CAMAC	TION	FOR	SEQ	ID :	NO :	29:								
		()	B) T C) S D) T	YPE: TRAN OPOL	H: 2: nuc. DEDN: OGY:	leic ESS: lin	acı sın ear	d d	3							,
	(ıi) MO	LECU	LE T	YPE:	CDN	A									
	(111) HY	POTH	ETIC	AL:	NC										
	(ili) AN	TI-S	ENSE	: NO											
	(vii				SOUR : HC		3									
	(1x	(AME/	KEY:											
	(xi) SE	QUEN	CE I	ESCR	IPTI	ON:	SEQ	ID N	10: 2	29:					
TA					AGC Ser 5											4.7
					n The					y Le					C CTG e Leu O	95
			Gl:	a Ala				s Ala	a Ar				a Pr	o Pr	C CCA o Pro	143
AG:	r TG	G GAC	3 E GAG C		g TG(G AAG	G TG	4. T CT		A CG	G CT	T AA	4 G CC		A CTA	191

Ser Trp Asp Glu Met Trp Lys Cys Leu Val Arg Leu Lys Pro Thr Leu 55 50

CAT GGA CCT ACG CCT CTT CTA TAT CGG TTG GGG CCT GTC CAA AAT GAA 239 His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Pro Val Gln Asn Glu

ATC TGC TTG ACA CAC CCC ATC ACA AAA TAC ATC ATG GCA TGC ATG TCA 287 Ile Cys Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala Cys Met Ser 90

- (2) INFORMATION FOR SEQ ID NO: 30:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 95 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO. 30.

Asp Phe Trp Glu Ser Val Phe Thr Gly Leu Thr His Ile Asp Ala His 5 1

Phe Leu Ser Gln Thr Lys Gln Gln Gly Leu Asn Phe Ser Phe Leu Thr

Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser 40 35

Trp Asp Glu Met Trp Lys Cys Leu Val Arg Leu Lys Pro Thr Leu His

Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Pro Val Glm Asm Glu Ile 70 65

Cys Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala Cys Met Ser 85

- (2) INFORMATION FOR SEQ ID NO: 31:
 - (i) SEQUENCE CHARACTERISTICS.
 - (A) LENGTH: 401 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (i11) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE: (B) CLONE: HD10-1-25

1221	FEATURE

(1x) FEATURE: (A) NAME/KEY: CDS

(B) LOCATION: 3..401

(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

TO CAA AAT GAA ATO TGO TTG ACA CAC COO GTO ACA AAA TAC ATT ATG Gln Asn Glu Ile Cys Leu Thr His Pro Val Thr Lys Tyr Ile Met 1 5 10 15	47
GCA TGC ATG TCA GCT GAT CTG GAA GTA ACC ACC AGC ACC TGG GTG TTG Ala Cys Met Ser Ala Asp Leu Glu Val Thr Thr Ser Thr Trp Val Leu 20 25 30	95
CTT GGA GGG GTC CTC GCG GCC CTA GCG GCC TAC TGC TTG TCA GTC GGC Leu Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Ser Val Gly 35 40 45	143
TGC GTT GTA ATC GTG GGT CAT ATC GAG CTG GGG GGC AAG CCG GCA CTC Cys Val Val Ile Val Gly His Ile Glu Leu Gly Gly Lys Pro Ala Leu 50 55 60	191
GTT CCA GAC AAG GAG GTG TTG TAT CAA CAG TAC GAT GAG ATG GAG GAG Val Pro Asp Lys Glu Val Leu Tyr Gln Gln Tyr Asp Glu Met Glu Glu 65 70 75	. 239
TGC TCG CAA GCC GCC CCA TAC ATC GAA CAA GCT CAG GTA ATA GCC CAC Cys Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala His 80 85 90 95	
CAG TTC AAG GAG AAA ATC CTT GGA CTG CTG CAG CGA GCC ACC CAA CAA Gln Phe Lys Glu Lys Ile Leu Gly Leu Leu Gln Arg Ala Thr Gln Gln 100 105 110	
CAA GCT GTC ATT GAG CCC GTA ATA GCT TCC AAC TGG CAA AAG CTT GAA Gln Ala Val Ile Glu Pro Val Ile Ala Ser Asn Trp Gln Lys Leu Glu 115 120 125	
ACC TTC TGG CAC AAG CAT Thr Phe Trp His Lys His 130	401

(2) INFORMATION FOR SEQ ID NO: 32:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH. 133 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (11) MOLECULE TYPE, protein
- (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

Gln Asn Glu Ile Cys Leu Thr His Pro Val Thr Lys Tyr Ile Met Ala 5 10

Cys	Met	Ser	Ala 20	Asp	Leu	Glu	Val	Thr 25	Thr	Ser	Thr	Trp	Val 30	Leu	Leu	
Gly	Gly	Val 35	Leu	Ala	Ala	Leu	Ala 40	Ala	Tyr	Суѕ	Leu	Ser 45	Val	Gly	Cys	
Val	Val 50	Ile	Val	Gly	Hıs	Ile 55	Glu	Leu	Gly	Gly	Lys 60	bro	Ala	Leu	Val	
Pro 65	Asp	Lys	Glu	Val	Leu 70	Tyr	Gln	Gln	Tyr	Asp 75	Glu	Met	Glu	Glu	Cys 80	
Ser	Gln	Ala	Ala	Pro 85	Tyr	Ile	Glu	Gln	Ala 90	Gln	Val	Ile	Ala	His 95	Gln	
Phe	Lys	Glu	Lys 100	Ile	Leu	Gly	Leu	Leu 105	Gla	Arg	Ala	Thr	Gln 110	Gln	Gln	-
		115	Glu		Val	Ile	Ala 120	Ser	Asn	Trp	Gln	Lys 125	Leu	Glu	Thr	Y
Phe	Trp 130	His	Lys	His												
(12)	(1) (ii (iii (iii (vii (vii) SE() (() (() () () () () () () () () () ()	QUENCA) LECUTO TI-ST MEDIA B) C ATUR A) N B) L	TE CEENGTE YPE: TRANT OPOLO ETIC ENSE ATE LONE AME/ OCAT	HARAGE A TOTAL TOT	CTER C1 b. leic ESS: lin cDN NO CE: 10-1 CDS 3	ISTI ase ; aci sin ear A	CS: pair d gle								
TC	CAA Gln	AAT	QUEN GAA Glu	ATC	TGC Cys	TTG	ACA	CAC	CCC	GTC Val	ACA				Met	47
					As <u>:</u>					Th					15 G TTC Lev	
							· ~~		~ ~~	o	a ma	a	~ m~	х с т	e eer	~ 14

								12	3								
Leu	Gly	Gly	Val 35	Leu	Ala	Ala	Leu	Ala 40	Ala	Tyr	Cia	Leu	Ser 45	Val	Gly		
TGC Cys	GTT Val	GTA Val 50	ATC Ile	GTG Val	GGT Gly	CAT His	ATC Ile 55	GAG Glu	CTG Leu	GGG Gly	GGC Gly	AAG Lys 60	CCG Pro	GCA Ala	CTC Leu		191
GTT Val	CCA Pro 65	GAC Asp	AAG Lys	GAG Glu	GTG Val	TTG Leu 70	TAT Tyr	CAA Gln	CAG Gln	TAC Tyr	GAT Asp 75	GAG Glu	ATG Met	GAG Glu	GAG Glu		239
TGC Cys 80	TCG Ser	CAA Gln	GCC Ala	GCC Ala	CCA Pro 85	TAC Tyr	ATC Ile	GAA Glu	CAA Gln	GCT Ala 90	CAG Gln	GTA Val	ATA Ile	GCC Ala	CAC His 95		237
CAG Gln	TTC Phe	AAG Lys	GAG Glu	AAA Lys 100	ATC Ile	CTT	GGA Gly	CTG Leu	CTG Leu 105	Gln	CGA Arg	GCC Ala	ACC Thr	CAA Gln 110	CAA Gln	-	335
CAA Gln	GCT Ala	GTC Val	ATT Ile 115	Glu	CCC	GTA Val	ATA Ile	GCT Ala 120	Ser	AAC Asn	TGG Trp	CAA Glm	AAG Lys 125	Leu	GAA Glu		383
			His	: AAG : Lys												,	401
(2)	INE	(1)	SEQU (A) I (B) 1	I FOR JENCE LENGI TYPE: TOPOI	CHP TH. 1	ARACT	TERI: amino acid	STICS	S: ids			•					
	(i:	1) M	OLECT	JLE :	TYPE	: pr	otei	n									
	(x	i) S	EQUE	NCE I	DESC	RIPT	ION:	SEQ	ID :	NO:	34:						

Gln Asn Glu Ile Cys Leu Thr His Pro Val Thr Lys Tyr Ile Met Ala

1 5 10 15

Cys Met Ser Ala Asp Leu Glu Val Thr Thr Ser Thr Trp Val Leu Leu 20 25 30

Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Ser Val Gly Cys 35 40 45

Val Val Ile Val Gly His Ile Glu Leu Gly Gly Lys Pro Ala Leu Val

Pro Asp Lys Glu Val Leu Tyr Gln Gln Tyr Asp Glu Met Glu Glu Cys
65 70 75 80

Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala His Gln 85 90 95

Phe Lys Glu Lys Ile Leu Gly Leu Leu Gln Arg Ala Thr Gln Gln Gln

			10	0				1	05				1	10					
Ala	Val	Ile		u P	ro V	al I	le A	la S 20	er A	sn T	zb G		ys L 25	eu (Glu	Th	r		
Phe	Trp 130	Hls	5 Ly	rs H	ıs														
(2)	INF	ORM	ATIC	N F	OR S	EQ I	D NO	: 35	:										
	(1		(A) (B) (C)	LEN TYP STR	GTH: E: n ANDE	401 ucle DNES	ERIS bas ic a Ss: s	e pa cid ingl	irs										
	(ıi) M	OLE	CULE	TYE	PE: c	AND												
	(i::) H	YPO	THET	ICAI	L: NO)											-	
	(iii	.) A	NTI	-SE	ISE:	NO													
	(vi:	.) I				OURC! BR3	E: 6-20	-164											
			(A) (B)	LC	ME/KI CATI		CDS 34		EQ 1	מו מב): 3 5	:							
TC.							TG A						LAA T	OA?	ATC	A?	:G		47
10	Gln 1	As:	n G2	iu I	le C	ys I 5	eu T	hr F	lis !	Pro 1	lle T	hr I	ys :	ryr	Ile	Me	15 15		
GC Al	A TG a Cy	C A s M	TG '	ICA Ser	GCT Ala 20	GAT Asp	CTG Leu	GAA Glu	GTA Val	ACC Thr 25	ACC Thr	AGC Ser	ACC Thr	TGG	Va	T :	rTG Leu		95
CT Le	T GG	A G y G	GG 1y	GTC Val 35	CTC Leu	GCG Ala	GCC Ala	CTA Leu	GCG Ala 40	Ala	TAC Tyr	TGC Cys	TTG Leu	TCA Ser 45	. Va	1	GGT Gly		143
TC Cy	st Gi vs Va	T G	TG al 50	ATT Ile	GTG Val	GGT Gly	CAT H1s	ATC Ile 55	Glu	CTG Leu	GGG Gly	GGC Gly	AAG Lys	Pro	G GC	IA La	ATC Ile		191
G7 Va	al P	CA (JAC Asp	AAA Lys	GAG Glu	GTG Val	TTG Leu 70	Tyr	CAP Glr	A CAP n Glr	TAC Tyr	GAT Asp 78) Git	ATO	G GZ t G	AA Lu	GAG Glu		239
T	GC T	CA (AAS	GCT	GCC	CCA	TAT	ATC	GA)	a CAJ	A GCT	CAC	GT	A AT	A G	CT	CAC		281

CAG TTC AAG GGA AAA GTC CTT GGA TTG CTG CAG CGA GCC ACC CAA CAA 335

Cys Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala His

85

80

Gln Phe Lys Gly Lys Val Leu Gly Leu Leu Gln Arg Ala Thr Gln Gln 100 105 110

CAA GCT GTC ATT GAG CCC ATA GTA ACT ACC AAC TGG CAA AAG CTT GAG
Gln Ala Val Ile Glu Pro Ile Val Thr Thr Asn Trp Gln Lys Leu Glu
115 120 125

GCC TTT TGG CAC AAG CAT Ala Phe Trp His Lys His 401

- (2) INFORMATION FCR SEQ ID NO: 36:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 133 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (11) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

Cys Met Ser Ala Asp Leu Glu Val Thr Thr Ser Thr Trp Val Leu Leu 20 25 30

Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Ser Val Gly Cys 40 45

Val Val Ile Val Gly His Ile Glu Leu Gly Gly Lys Pro Ala Ile Val 50 60

Pro Asp Lys Glu Val Leu Tyr Gln Gln Tyr Asp Glu Met Glu Glu Cys
65 75 80

Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Vai Ile Ala His Gln 85 90 95

Phe Lys Gly Lys Val Leu Gly Leu Leu Gln Arg Ala Thr Gln Gln Gln 100 105 110

Ala Val Ile Glu Pro Ile Val Thr Thr Asn Trp Gin Lys Leu Glu Ala 115 120 125

Phe Trp His Lys His 130

- (2) INFORMATION FOR SEQ ID NO: 37:
 - (1) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 401 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

123	
(11) MOLECULE TYPE: cDNA	
(111) HYPOTHETICAL: NO	
(lil) ANTI-SENSE: NO	
(V11) IMMEDIATE SOURCE: (B) CLONE: BR36-20-166	
(1x) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 3401	
(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 37:	
TC CAA AAT GAA ATC TGC TTG ACA CAC CCC ATC ACA AAA TAC ATC ATG Glm Asn Glu Ile Cys Leu Thr His Pro Ile Thr Lys Tyr Ile Met 1 5 10 15	47
GCA TGC ATG TCA GCT GAT CTG GAA GTA ACC ACC AGC ACC TGG GTT TTG Ala Cys Met Ser Ala Asp Leu Glu Val Thr Thr Ser Thr Trp Val Leu 20 25 30	95
CTT GGA GGG GTC CTC GCG GCC CTA GCG GCC TAC TGC TTG TCA GTC GGT Leu Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Ser Val Gly 35 40 45	143
TGT GTT GTG ATT GTG GGT CAT ATC GAG CTG GGG GGC AAG CCG GCA ATC Cys Val Val Ile Val Gly His Ile Glu Leu Gly Gly Lys Pro Ala Ile 50 55 60	191
GTT CCA GAC AAA GAG GTG TTG TAT CAA CAA TAC GAT GAG ATG GAA GAG Val Pro Asp Lys Glu Val Leu Tyr Gln Gln Tyr Asp Glu Met Glu Glu 65 70 75	239
TGC TCA CAA GCT GCC CCA TAT ATC GAA CAA GCT CAG GTG ATA GCT CAC Cys Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala His 80 85 90 95	297
CAG TTC AAG GAA AAA GTC CTT GGA TTG CTG CAG CGA GCC ACC CAA CAA Gln Phe Lys Glu Lys Val Leu Gly Leu Gln Arg Ala Thr Gln Gln 100 105 110	335
CAA GCT GTC ATT GAG CCC ATA GTA ACT ACC AAC TGG CAA AAG CTT GAG Gln Ala Val Ile Glu Pro Ile Val Thr Thr Asn Trp Gln Lys Leu Glu 115 120 125	383
GCC TTT TGG CAC AAG CAT Ala Phe Trp His Lys His 130	401

- (2) INFORMATION FOR SEQ ID NO: 38.
 - (i) SEQUENCE CHARACTERISTICS:

- (B) TYPE: amino acid
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:

Gln Asn Glu Ile Cys Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala 1 5 10 15

Cys Met Ser Ala Asp Leu Glu Val Thr Thr Ser Thr Trp Val Leu Leu 20 25 30

Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Ser Val Gly Cys 45

Val Val Ile Val Gly His Ile Glu Leu Gly Gly Lys Pro Ala Ile Val 50 60

Pro Asp Lys Glu Val Leu Tyr Gln Gln Tyr Asp Glu Met Glu Glu Cys 65 70 75 80

Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala His Gln 85 90 95

Phe Lys Glu Lys Val Leu Gly Leu Leu Gln Arg Ala Thr Gln Gln Gln 100 105 110

Ala Val Ile Glu Pro Ile Val Thr Thr Asn Trp Gln Lys Leu Glu Ala 115 120 125

Phe Trp His Lys His

- (2) INFORMATION FOR SEQ ID NO: 39:
 - (i) SEQUENCE CHARACTERISTICS.
 - (A) LENGTH: 401 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:

(B) CLONE: BR36-20-165

- (1x) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 3..401
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

		AAA TAC ATC ATG Lys Tyr Ile Met 15	47
		C ACC TGG GTT TTG r Thr Trp Val Leu 30	95
		C TTG TCA GTC GGT rs Leu Ser Val Gly 43	143
	Glu Leu Gly Gl	C AAG CCG GCA ATC y Lys Pro Ala Ile 60	191
	Gin Gin Tyr As	AT GAG ATG GAA GAG p Glu Met Glu Glu 5	- 239
		AG GTA ATA GCT CAC In Val Ile Ala His 95	287
		SA GCC ACC CAA CAA rg Ala Thr Gln Gln 110	335
		eg CAA AAG CTT GAG pp Gln Lys Leu Glu 125	383
GCC TTT TGG CAC Ala Phe Trp His 130			401

(2) INFORMATION FOR SEQ ID NO: 40:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 133 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (11) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:

Gln Asn Glu Ile Cys Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala 1 10 15

Cys Met Ser Ala Asp Leu Glu Val Thr Thr Ser Thr Trp Val Leu Leu 20 25 30

Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Ser Val Gly Cys 45

Val Val Ile Val Gly His Ile Glu Leu Gly Gly Lys Pro Ala Ile Val

val Val He Val Gly His He Glu Leu Gly Gly Ly 50 55 6	'S Pro Ala Ile Val O
Pro Asp Lys Glu Val Leu Tyr Gln Gln Tyr Asp Gl 65 70 75	u Met Glu Glu Cys 80
Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Va 85 90	il Ile Ala His Gln 95
Phe Lys Glu Lys Val Leu Gly Leu Leu Gln Arg Al 100 . 105	a Thr Gln Gln Gln 110
Ala Val Ile Glu Pro Ile Val Thr Thr Asn Trp Gl. 115 120	n Lys Leu Glu Ala 125
Phe Trp His Lys His 130	
(2) INFORMATION FOR SEQ ID NO: 41:	-
 (1) SEQUENCE CHARACTERISTICS: (A) LENGTH: 509 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(11) MOLECULE TYPE: dDNA	
(iii) HYPOTHETICAL: NO	
(iii) ANTI-SENSE: NO	
(vii) IMMEDIATE SOURCE: (B) CLONE: PC-2-1	
(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 3509	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:	
CC ATG AGC ACG AAT CCT AAA CCT CAA AGA AAA ACC Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr 1 5 10	AAA AGA AAC ACC 47 Lys Arg Asn Thr
AAC CGT CGC CCA CAG GAC GTC AAG TTC CCG GGC GG Asn Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gl 20 25	ST GGT CAG ATC GTT 95 .y Gly Gln Ile Val 30
GGC GGA GTT TAC TTG TTG CCG CGC AGG GGC CCT AG Gly Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Ar 35 40	GG ATG GGT GTG CGC 143 Fg Met Gly Val Arg 45
GCG ACT CGG AAG ACT TCG GAA CGG TCG CAA CCC CG Ala Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Ar	

		50					55					60					
CCT Pro	ATT Ile 65	CCC Pro	AAG Lys	GCG Ala	CGC	CAG Gln 70	CCC	ACG Thr	GGC Gly	CGG Arg	TCC Ser 75	TGG Trp	GGT Gly	CAA Gln	CCC Pro		239
GGG Gly 80	TAC Tyr	CCT Pro	TGG Trp	Pro	CTT Leu 85	TAC Tyr	GCC Ala	AAT Asn	GAG Glu	GGC Gly 90	CTC Leu	GGG Gly	Trp TGG	GCA Ala	GGG Gly 95		287
TGG Trp	CTG Leu	CTC Leu	TCC Ser	CCT Pro 100	Arg	GC	TCT Ser	Y zâ C@@	CCT Pro 105	AAT Asn	TGG Trp	GGC Gly	CCC Pro	AAT Asn 110	GAC Asp		335
CCC Pro	CGG Arg	CGA Arg	AAA Lys 115	TCG Ser	CGT Arg	AAT Asn	TTG Leu	GGT Gly 120	AAG Lys	GTC Val	ATC Ile	GAT Asp	ACC Thr 125	CTA Leu	ACG Thr		3 83
TGC Cys	GGA Gly	TTC Phe 130	GCC Ala	GAT Asp	CTC Leu	ATG Met	GGG Gly 135	TAT Tyr	ATC Ile	CCG Pro	CTC Leu	GTA Val 140	GGC Gly	GGC Gly	Dzo CCC	•	431
ATT Ile	GGG Gly 145	GGC Gly	GTC Val	GCA Ala	AGG Arg	GCT Ala 150	CTC Leu	GCA Ala	CAC H1s	GGT Gly	GTG Val 155	AGG Arg	GTC Val	CTT Leu	GAG Glu		4 79
			AAC Asn														509
(2)	t.	(i) S () 2) (I)	CION SEQUE A) LE B) TO	ENCE ENGTI (PE : DPCL	CHAI H: 16 amii DGY:	RACTI 69 ar 10 ac	ERIST mino Did Bar	rics									
Mot			NSU.					-				3	2	m>	3		
1	361	111-	ASI.	5	nys	PIO	GIII	Arg	10	THE	rys	Arg	AST	1nr 15	AST		
Arg	Arg	Pro	Gln 20	Asp	Val	Lys	Phe	Pro 25	Gly	Gly	Gly	Gln	Ile 30	Val	Gly		
Gly	Val	Tyr 35	Leu	Leu	Pro	Arg	Arg 40	Gly	Pro	Arg	Met	Gly 45	Val	Arg	Ala		
Thr	Arg 50	Lys	Thr	Ser	Glu	Arg 55	Ser	Gln	Pro	Arg	Gly 60	Arg	Arg	Gln	Pro		
Ile 65	Pro	Lys	Ala	Arg	Gln 70	Pro	Thr	Gly	Arg	Ser	Trp	Gly	Gln	Pro	Gly		

65 70 75 80

Tyr Pro Trp Pro Leu Tyr Ala Asn Glu Gly Leu Gly Trp Ala Gly Trp

85		90		95
Leu Leu Ser Pro Arg 100	Gly Ser Arg	Pro Asn Trp 105	Gly Pro Asn 110	Asp Pro
Arg Arg Lys Ser Arg	Asn Leu Gly 120	Lys Val Ile	Asp Thr Leu 125	Thr Cys
Gly Phe Ala Asp Leu 130	Met Gly Tyr 135	Ile Pro Leu	Val Gly Gly 140	Pro Ile
Gly Gly Val Ala Arg 145	Ala Leu Ala 150	His Gly Val	Arg Val Leu	Glu Asp 160
Gly Val Asn Tyr Ala 165	Thr Gly Asn	Leu		
(2) INFORMATION FOR	SEQ ID NO:43	3 :		-
(B) TYPE: (C) STRANT	HARACTERISTIC H: 509 base p nucleic acid DEDNESS: sing DGY: linear	pairs i		
(i1) MOLECULE TO	(PE: cDNA			•
(iii) HYPOTHETICA	VI: NO			
(iii) ANTI-SENSE	: NO			
(vii) IMMEDIATE S (B) CLONE:				
(ix) FEATURE: (A) NAME/! (B) LOCAT!	CEY: CDS ION: 3509			
(xi) SEQUENCE DE	ESCRIPTION: 8	SEQ ID NO: 4	3:	
CC ATG AGC ACG AAT C Met Ser Thr Asn I 1				
AAC CGT CGC CCA CAG Asn Arg Arg Pro Gln 20				
GGC GGA GTT TAC TTG Gly Gly Val Tyr Leu 35				

Ala Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln

55

50

GCG ACT CGG AAG ACT TCG GAA CGG TCG CAA CCC CGT GGA CGG CGT CAG 191

60

CCT Pro	ATT Ile 65	CCC Pro	AAG Lys	GCG Ala	CGC Arg	CAG Gln 70	Pro CCC	ACG Thr	GGC Gly	CGG Ar g	TCC Ser 75	TGG Trp	GGT Gly	CAA Gln	CCC Pro		239
GGG Gly 8 0	TAC Tyr	CCT Pro	TGG Trp	CCC Pro	CTT Leu 85	TAC Tyr	GCC Ala	AAT Asn	GAG Glu	GGC Gly 90	CTC	GGG Gly	TGG Trp	GCA Ala	GGG Gly 95		287
TGG Trp	CTG Leu	CTC Leu	TCC Ser	CCT Pro 100	CGA Arg	GGC Gly	TCT Ser	Yra Cee	CCT Pro 105	AAT Asn	dzī Dec	GGC Gly	CCC	AAT Asn 110	GAC Asp		335
CCC Pro	CGG Arg	CGA Arg	AAA Lys 115	TCG Ser	CGT Arg	AAT Asn	TTG Leu	GGT Gly 120	AAG Lys	GTC Val	ATC Ile	GAT Asp	ACC Thr 125	CTA Leu	ACG Thr		383
TGC Cys	GGA Gly	TTC Phe 130	GCC ['] Ala	GAT Asp	CTC Leu	ATG Met	GGG Gly 135	TAT Tyr	ATC Ile	CCG Pro	CTC Leu	GTA Val 140	GGC Gly	GGC Gly	CCC Pro	-	431
ATT Ile	GGG Gly 145	GGC Gly	GTC Val	GCA Ala	AGG Arg	GCT Ala 150	CTC	GCA Ala	CAC His	GGT Gly	GTG Val 155	AGG Arg	GTC Val	CTT Leu	GAG Glu		479.
					GCA Ala 165											,	509

(2) INFORMATION FOR SEQ ID NO: 44:

- (1) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 169 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (11) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 44:

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn 1 5 10 15

Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly
20 25 30

Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Met Gly Val Arg Ala 35 40 45 .

Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro 50 55 60

Ile Pro Lys Ala Arg Gln Pro Thr Gly Arg Ser Trp Gly Gln Pro Gly 65 70 75 80

Tyr Pro Trp Pro Leu Tyr Ala Asn Glu Gly Leu Gly Trp Ala Gly Trp 85 90 95

Leu	Leu	Ser	Pro 100	Arg	Gly	Ser	Arg	Pro 105	Asn	Trp	Gly	Pro	Asn 110	Asp	Pro	
Arg	Arg	Lys 115	Ser	Arg	Asn	Leu	Gly 120	Lys	Val	Ile	qzA	Thr 125	Leu	Thr	Cys	
Gly	Phe 130	Ala	Asp	Leu	Mec	Gly 135	Tyr	Ile	Pro	Leu	Val 140	Gly	Gly	Pro	Ile	
Gly 145	Gly	Val	Ala	Arg	AL a 150	Lau	Ala	His	Gly	Val 155	۸۳3	Val	Leu	Glu	Asp 160	
Gly	Val	Asn	Tyr	Ala 165	Thr	Gly	Asn	Leu								
(2)		SEC	QUENC	E C	iarac	ID N	STIC	CS:								-
		(E	3) TY C) S7	PE : Rani	באכם מעכם	0 ba elc ESS: line	acio	i	5							
	(ii)	MOI	LECUI	E T	PE:	CDNA										,
	(iii)	HYE	POTHE	TIC	۱. ۱۲	iC										
	(iii)	ANT	TI-SE	INSE:	NO.											
	(vii)		MEDIA 3) CL													
	(ix)	(P	TURE L) NA B) LC	ME/:		CDS 25	80									
	(xi)	SEÇ	UENC	E DE	SCRI	PTIC	N: S	EQ I	D NO): 45	i :					
A AC	G TG ir Cy 1	C GG s Gl	A TI .y Ph	C GC Le Al	C GA .a As 5	T CT	C AT	G GG	y Ty	AT AT	CC CC .e Pr	G CT	'C GI	l Gl	Ю У .5	46
GGC Gly	CCC Pro	ATT Ile	GGG Gly	GGC Gly 20	GTC Val	GCA Ala	AGG Arg	GCT Ala	CTC Leu 25	GCA Ala	CAC H1s	GGT Gly	GTG Val	AGG Arg 30	GTC Val	94
Leu	Glu	Asp	Gly 35	Val	Asn	TAT Tyr	Ala	Thr 40	Gly	Asn	Leu	czą	Gly 45	Cys	Ser	142
TTC Phe	TCT Ser	ATC Ile 50	TTT Phe	ATT Ile	CTT Leu	GCT Ala	CTT · Leu 55	CTC Leu	TCG Ser	TGT Cys	CTG Leu	ACC Thr 60	GTT Val	CCG Pro	GCC Ala	190
TCT	GCA	GTT	CCC	TAC	CGA	AAT	GCC	TCT	GGG	ATT	TAT	CAT	GTT	ACC	AAT	238

Ser	Ala 65	Val	Pro	Tyr	Arg	Asn 70	Ala	Ser	Gly	Ile	Tyr 75	Hıs	Val	Thr	Asn		
GAT Asp 80	TGC Cys	CCA Pro	AAC Asn	TCT Ser	TCC Ser 85	ATA Ile	GTC Val	TAT Tyr	GAG Glu	GCA Ala 90	GAT Asp	AAC Asn	CTG Leu	ATC Ile	CTA Leu 95		286
			GGT Gly														334
			CAA Gln 115														382
			CCT Pro														430
			TCC Ser														478
			CAA Gln													ř	526
			AAC Asn														574
ATG Met																	580

(2) INFORMATION FOR SEQ ID NO: 46:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 46:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly
1 10 15

Pro Ile Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu 20 25 30

Glu Asp Gly Val Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

Ser Ile Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55 60

Ala Val Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asn Leu Ile Leu His
85 90 95

Ala Pro Gly Cys Val Pro Cys Val Met Thr Gly Asn Val Ser Arg Cys 100 105 110

Trp Val Gln Ile Thr Pro Thr Leu Ser Ala Pro Ser Leu Gly Ala Val

Thr Ala Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala Gly Gly Ala Ala 130 135 140

Leu Cys Ser Ala Leu Tyr Val Gly Asp Ala Cys Gly Ala Leu Phe Leu 145 150 155 160

Val Gly Gln Met Phe Thr Tyr Arg Pro Arg Gln His Ala Thr Val Gln 165 170 175

Asn Cys Asn Cys Ser Ile Tyr Ser Gly His Val Thr Gly His Arg Met 180 185 190

Ala

- (2) INFORMATION FOR SEQ ID NO: 47:
 - (1) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 580 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - . (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: PC-4-5
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 2..580
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:

A ACG TGC GGA TTC GCC GAT CTC ATG GGG TAT ATC CCG CTC GTA GGC
Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly
1 5 10

GGC CCC ATT GGG GGC GTC GCA AGG GCT CTC GCA CAC GGT GTG AGG GTC

94

46

Gly	Pro	Ile	Gly	Gly 20	Val	Ala	Arg	Aia	Leu 25	Ala	His	Gly	Val	Arg 30	Val		
CTT Leu	GAG Glu	GAC Asp	GGG Gly 35	GTA Val	AAC Asn	TAT Tyr	GCA Ala	ACA Thr 40	GGG Gly	AAT Asn	TTA Leu	CCC	GGT Gly 45	TGC Cys	TCT Ser		142
TTC Phe	TCT Ser	ATC Ile 50	TTT	ATT Ile	CTT	GCT Ala	CTT Leu 55	CTC Leu	TCG Ser	Cha	CTG Leu	ACC Thr 60	GTT Val	CCG Pro	GCC Ala		190
TCT Ser	GCA Ala 65	GTT Val	CCC	TAC Tyr	CGA Arg	AAT Asn 70	GCC Ala	TIT Ser	GGG Gly	ATT Ile	TAT Tyr 75	CAT His	GTT Val	ACC Thr	AAT Asn		238
GAT Asp 80	TGC Cys	CCA Pro	AAC Asn	TCT Ser	TCC Ser 85	ATA Ile	GTC Val	TAT Tyr	GAG Glu	GCA Ala 90	GAT Asp	AAC Asn	CTG Leu	ATC Ile	CTA Leu 95	-	286
CAC His	GCA Ala	CCT Pro	GGT Gly	TGC Cys 100	GTG Val	CCT Pro	TGT Cys	GTC Val	ATG Mer 105	ACA Thr	GGT Gly	AAT Asn	GTG Val	AGT Ser 110	AGA Arg		334
TGC Cys	TGG Trp	GTC Val	CAA Gln 115	ATT Ile	ACC Thr	CCT Pro	ACA Thr	CTG Leu 120	TCA Ser	GCC Ala	CC3 Pro	AGC Ser	CTC Leu 125	GGA Gly	GCA Ala		382
GTC Val	ACG Thr	GCT Ala 130	CCT Pro	CTT Leu	Yr3 CGG	AGA Arg	GCC Ala 135	GTT Val	GAC Asp	TAC Tyr	CTA L eu	GCG Ala 140	GGA Gly	GGG Gly	GCT Ala		430
GCC Ala	CTC Leu 145	TGC Cys	TCC Ser	GCG Ala	TTA Leu	TAC Tyr 150	GTA Val	GGA Gly	GAC Asp	GCG Ala	TGT Cys 155	GGG Gly	GCA Ala	CTA Leu	TTC Phe		478
TTG Leu 160	GTA Val	GGC Gly	CAA Gln	ATG Met	TTC Phe 165	ACC Thr	TAT Tyr	AGG Arg	Sto	CGC Arg 170	CAG Gln	CAC His	GCT Ala	ACG Thr	GTG Val 175		526
CAG Gln	AAC Asn	TGC Cys	AAC Asn	TGT Cys 180	TCC Ser	ATT Ile	TAC Tyr	AGT Ser	GGC Gly 185	CAT His	GTT Val	ACC Thr	GGC Gly	CAC His 190	CGG Arg		574
ATG Met																	580

(2) INFORMATION FOR SEQ ID NO: 48:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear -
- (i1) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly
1 5 10 15

Pro Ile Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu
20 25 30

Glu Asp Gly Val Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

Ser Ile Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55 60

Ala Val Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asn Leu Ile Leu His 85 90 95

Ala Pro Gly Cys Val Pro Cys Val Met Thr Gly Asn Val Ser Arg Cys
100 105 110

Trp Val Gln Ile Thr Pro Thr Leu Ser Ala Pro Ser Leu Gly Ala Val 115 120 125

Thr Ala Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala Gly Gly Ala Ala 130 140

Leu Cys Ser Ala Leu Tyr Val Gly Asp Ala Cys Gly Ala Leu Phe Leu 145 150 155 160

Val Gly Gln Met Phe Thr Tyr Arg Pro Arg Gln His Ala Thr Val Gln 165 170 175

Asn Cys Asn Cys Ser Ile Tyr Ser Gly His Val Thr Gly His Arg Met 180 185 190

Ala

- (2) INFORMATION FOR SEQ ID NO: 49:
 - (1) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 959 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (11) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (111) ANTI-SENSE. NO
 - (vii) IMMEDIATE SOURCE:
 (B) CLONE: PC-3-4

(1x) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 3..959

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49.

CC ATG AGC ACG AAT CCT AAA CCT CAA AGA AAA ACC AAA AGA AAC ACC Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr 1 5 10 15	47
AAC CGT CGC CCA CAG GAC GTC AAG TTC CCG GGC GGT GGT CAG ATC GTT Asn Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val 20 25 30	95
GGC GGA GTT TAC TTG TTG CCG CGC AGG GGC CCT AGG ATG GGT GTG CGC Gly Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Met Gly Val Arg 35 40 45	143
GCG ACT CGG AAG ACT TCG GAA CGG TCG CAA CCC CST GGA CGG CGT CAG Ala Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln 50 55 60	191
CCT ATT CCC AAG GCG CGC CAG CCC ACG GGC CGG TCC TGG GGT CAA CCC Pro Ile Pro Lys Ala Arg Gln Pro Thr Gly Arg Ser Trp Gly Gln Pro 65 70 75	239
GGG TAC CCT TGG CCC CTT TAC GCC AAT GAG GGC CTC GGG TGG GCA GGG Gly Tyr Pro Trp Pro Leu Tyr Ala Asn Glu Gly Leu Gly Trp Ala Gly 80 85 90 95	287
TGG CTG CTC CCT CGA GGC TCT CGG CCT AAT TGG GGC CCC AAT GAC Trp Leu Leu Ser Pro Arg Gly Ser Arg Pro Asn Trp Gly Pro Asn Asp 100 105 110	335
CCC CGG CGA AAA TCG CGT AAT TTG GGT AAG GTC ATC GAT ACC CTA ACG Pro Arg Arg Lys Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr 115 120 125	383
TGC GGA TTC GCC GAT CTC ATG GGG TAT ATC CCG CTC GTA GGC GGC CCC Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly Pro 130 135 140	431
ATT GGG GGC GTC GCA AGG GCT CTC GCA CAC GGT GTG AGG GTC CTT GAG Ile Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu Glu 145 150 155	479
GAC GGG GTA AAC TAT GCA ACA GGG AAT TTA CCC GGT TGC TCT TTC TCT Asp Gly Val Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe Ser 160 165 170 175	527
ATC TTT ATT CTT GCT CTT CTC TCG TGT CTG ACC GTT CCG GCC TCT GCA Ile Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser Ala 180 185 190	575
GTT CCC TAC CGA AAT GCC TCT GGG ATT TAT CAT GTT ACC AAT GAT TGC Val Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp Cys 195 200 205	

				GCA Ala						67	1
				ACA Thr						71	9
				GCC Ala			 			76	7
				TAC Tyr			 			81	5
		 		GCG Ala 280			 	GTA Val	-	86	3
				CGC Arg						91	1
		 					 	GCA Ala	,	95	Э

(2) INFORMATION FOR SEQ ID NO: 50:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 319 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50:

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn

1 10 15

Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly
20 25 30

Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Met Gly Val Arg Ala

Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro 50 55 60

Ile Pro Lys Ala Arg Gln Pro Thr Gly Arg Ser Trp Gly Gln Pro Gly 65 70 75 80

Tyr Pro Trp Pro Leu Tyr Ala Asn Glu Gly Leu Gly Trp Ala Gly Trp 85 90 95

- Leu Leu Ser Pro Arg Gly Ser Arg Pro Asn Trp Gly Pro Asn Asp Pro
 100 105 110
- Arg Arg Lys Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys 115 120 125
- Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly Pro Ile 130 140
- Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu Glu Asp 145 150 155 160
- Gly Val Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe Ser Ile 165 170 175
- Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser Ala Val 180 185 190
- Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp Cys Pro 195 200 205
- Asn Ser Ser Ile Val Tyr Glu Ala Asp Asn Leu Ile Leu His Ala Pro 210 215 220
- Gly Cys Val Pro Cys Val Met Thr Gly Asn Val Ser Arg Cys Trp Val 225 230 235 240
- Gln Ile Thr Pro Thr Leu Ser Ala Pro Ser Leu Gly Ala Val Thr Ala 245 250 255
- Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala Gly Gly Ala Ala Leu Cys 260 265 270
- Ser Ala Leu Tyr Val Gly Asp Ala Cys Gly Ala Leu Phe Leu Val Gly 275 280 285
- Gln Met Phe Thr Tyr Arg Pro Arg Gln His Ala Thr Val Gln Asn Cys 290 295 300
- Asn Cys Ser Ile Tyr Ser Gly His Val Thr Gly His Arg Met Ala 305
- (2) INFORMATION FOR SEQ ID NO: 51:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 959 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (11) MOLECULE TYPE: cDNA
 - (111) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:

(B) CLONE: PC-3-8

(ix) FEATURE:

(A) NAME/KEY: CDS
(B) LCCATION: 3..959

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 51:

CC ATG AGC ACG AAT CCT AAA CCT CAA AGA AAA ACC AAA AGA AAC ACC Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr 1 5 10 15	47
AAC CGT CGC CCA CAG GAC GTC AAG TTC CCG GGC GGT GGT CAG ATC GTT Asn Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val 20 25 30	95
GGC GGA GTT TAC TTG TTG CCG CGC AGG GGC CCT AGG ATG GGT GTG CGC-Gly Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Met Gly Val Arg 45	143
GCG ACT CGG AAG ACT TCG GAA CGG TCG CAA CCC CGT GGA CGG CGT CAG Ala Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln 50 55 60	191
CCT ATT CCC AAG GCG CGC CAG CCC ACG GGC CGG TCC TGG GGT CAA CCC Pro Ile Pro Lys Ala Arg Gln Pro Thr Gly Arg Ser Trp Gly Gln Pro 65 70 75	239
GGG TAC CCT TGG CCC CTT TAC GCC AAT GAG GGC CTC GGG TGG GCA GGG Gly Tyr Pro Trp Pro Leu Tyr Ala Asn Glu Gly Leu Gly Trp Ala Gly 80 85 90 95	287
TGG CTG CTC TCC CCT CGA GGC TCT CGG CCT AAT TGG GGC CCC AAT GAC Trp Leu Leu Ser Pro Arg Gly Ser Arg Pro Asn Trp Gly Pro Asn Asp 100 105 110	335
CCC CGG CGA AAA TCG CGT AAT TTG GGT AAG GTC ATC GAT ACC CTA ACG Pro Arg Arg Lys Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr 115 120 125	383
TGC GGA TTC GCC GAT CTC ATG GGG TAC ATC CCG CTC GTA GGC GGC CCC Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly Pro 130 135 140	431
GTT GGG GGC GTC GCA AGG GCT CTC GCA CAC GGT GTG AGG GTC CTT GAG Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu Glu 145 150 155	4 79
GAC GGG GTA AAC TAT CCA ACA GGG AAT TTA CCC GGT TGC TCT TTC TCT Asp Gly Val Asn Tyr Pro Thr Gly Asn Leu Pro Gly Cys Ser Phe Ser 160 165 170 175	527
ATC TTT ATT CTT GCT CTC TCG-TGT CTG ACC GTT CCG GCC TCT GCA Ile Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser Ala 180 185 190	575
GTT CCC TAC CGA AAT GCC TCT GGG ATT TAT CAT GTT ACC AAT GAT TGC	623

Val	Pro	Tyr	Arg 195	Asn	Ala	Ser	Gly	Ile 200	Tyr	His	Val	Thr	Asn 205	Asp	Cys		
CCA Pro	AAC Asn	TCT Ser 210	TCC Ser	ATA Ile	GTC Val	TAT Tyr	GAG Glu 215	GCA Ala	GAT Asp	AAC Asn	CTG Leu	ATC Ile 220	CTA Leu	CAC His	GCA Ala		671
CCT Pro	GGT Gly 225	TGC Cys	GTG Val	CCT	TGT Cys	GTC Val 230	ATG Met	ACA Thr	GGT Gly	AAT Asn	GTG Val 235	AGT Ser	AGA Arg	TGC Cys	TGG Trp		719
GTC Val 240	CAA Gln	ATT Ile	ACC Thr	Pro	ACA Thr 245	CTG Leu	TCA Ser	GCC Ala	CCG Pro	AGC Ser 250	CTC Leu	GGA Gly	GCA Ala	GTC Val	ACG Thr 255		767
														GCC Ala 270		_	815
														TTG Leu			863
														CAG Gln			911
														ATG Met			959

(2) INFORMATION FOR SEQ ID NO: 52:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 319 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (11) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn 1 5 10 15

Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly 20 25 30 .

Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Met Gly Val Arg Ala 35 40 45

Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro 50 60

Ile Pro Lys Ala Arg Gln Pro Thr Gly Arg Ser Trp Gly Gln Pro Gly 65 70 75 80

- Tyr Pro Trp Pro Leu Tyr Ala Asn Glu Gly Leu Gly Trp Ala Gly Trp 85 90 95
- Leu Leu Ser Pro Arg Gly Ser Arg Pro Asn Trp Gly Pro Asn Asp Pro 100 105 110
- Arg Arg Lys Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys 115 120 125
- Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly Pro Val 130 135 140
- Gly Val Asn Tyr Pro Thr Gly Asn Leu Pro Gly Cys Ser Phe Ser Ile 165 170 175
- Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser Ala Val 180 185 190
- Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp Cys Pro 195 200 205
- Asn Ser Ser Ile Val Tyr Glu Ala Asp Asn Leu Ile Leu His Ala Pro 210 215 220
- Gly Cys Val Pro Cys Val Met Thr Gly Asn Val Ser Arg Cys Trp Val 225 230 235 240
- Gln Ile Thr Pro Thr Leu Ser Ala Pro Ser Leu Gly Ala Val Thr Ala 245 250 255
- Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala Gly Gly Ala Ala Leu Cys 260 265 270
- Ser Ala Leu Tyr Val Gly Asp Ala Cys Gly Ala Leu Phe Leu Val Gly 275 280 285
- Gln Met Phe Thr Tyr Arg Pro Arg Gln His Ala Thr Val Gln Asn Cys 290 295 300
- Asn Cys Ser Ile Tyr Ser Gly His Val Thr Gly His Arg Met Ala 305 315
- (2) INFORMATION FOR SEQ ID NO: 53:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 959 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (11) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO

- (ill) ANTI-SENSE: NO
- (vii) IMMEDIATE SOURCE:
 (B) CLONE: PC C/E1
- (1x) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..959
- (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 53:

CCATGAGCAC	GAATCCTAAA	CCTCAAAGAA	AAACCAAAAG	AAACACCAAC	CGTCGCCCAC	60
AGGACGTCAA	GTTCCCGGGC	GGTGGTCAGA	TCGTTGGCGG	AGTTTACTTG	TTGCCGCGCA	120
GGGGCCCTAG	GATGGGTGTG	CGCGCGACTC	GGAAGACTTC	GGAACGGTCG	CAACCCCGTG -	130
GACGGCGTCA	GCCTATTCCC	AAGGCGCGCC	AGCCCACGGG	CCGGTCCTGG	GGTCAACCCG	240
GGTACCCTTG	GCCCCTTTAC	GCCAATGAGG	GCCTCGGGTG	GGCAGGGTGG	CTGCTCTCCC	300
CTCGAGGCTC	TCGGCCTAAT	TGGGGCCCCA	ATGACCCCCG	GCGAAAATCG	CGTAATTTGG	350
GTAAGGTCAT	CGATACCCTA	ACGTGCGGAT	TCGCCGATCT	CATGGGGTAY	ATCCCGCTCG	420
TAGGCGGCCC	CRTTGGGGGC	GTCGCAAGGG	CTCTCGCACA	CGGTGTGAGG	GTCCTTGAGG	480
ACGGGGTAAA	CTATSCAACA	GGGAATTTAC	CCGGTTGCTC	TTTCTCTATC	TTTATTCTTG	540
CTCTTCTCTC	GTGTCTGACC	GTTCCGGCCT	CTGCAGTTCC	CTACCGAAAT	GCCTCTGGGA	600
TTTATCATGT	TACCAATGAT	TGCCCAAACT	CTTCCATAGT	CTATGAGGCA	GATAACCTGA	650
TCCTACACGC	ACCTGGTTGC	GTGCCTTGTG	TCATGACAGG	TAATGTGAGT	AGATGCTGGG	720
TCCAAATTAC	CCCTACACTG	TCAGCCCCGA	GCCTCGGAGC	AGTCACGGCT	CCTCTTCGGA	780
GAGCCGTTGA	CTACCTAGCG	GGAGGGGCTG	CCCTCTGCTC	CGCGTTATAC	GTAGGAGACG	840
CGTGTGGGGC	ACTATTCTTG	GTAGGCCAAA	TGTTCACCTA	TAGGCCTCGC	CAGCACGCTA	900
CGGTGCAGAA	CTGCAACTGT	TOCATTTACA	GTGGCCATGT	TACCGGCCAC	CGGATGGCA	959

- (2) INFORMATION FOR SEQ ID NO: 54:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 319 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (11) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54.

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn $1 \hspace{1.5cm} 5 \hspace{1.5cm} 10 \hspace{1.5cm} 15$

- Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly
 20 25 30
- Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Met Gly Val Arg Ala
 35 40 45
- Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro 50 55 60
- Ile Pro Lys Ala Arg Gln Pro Thr Gly Arg Ser Trp Gly Gln Pro Gly 65 70 75 80
- Tyr Pro Trp Pro Leu Tyr Ala Asn Glu Gly Leu Gly Trp Ala Gly Trp 85 90 95
- Leu Leu Ser Pro Arg Gly Ser Arg Pro Asn Trp Gly Pro Asn Asp Pro 100 105 110
- Arg Arg Lys Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys 115 120 125
- Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly Pro Val 130 135 140
- Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu Glu Asp 145 150 155 160
- Gly Val Asn Tyr Pro Thr Gly Asn Leu Pro Gly Cys Ser Phe Ser Ile 165 170 175
- Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser Ala Val 180 185 190
- Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp Cys Pro 195 200 205
- Asn Ser Ser Ile Val Tyr Glu Ala Asp Asn Leu Ile Leu His Ala Pro 210 215 220
- Gly Cys Val Pro Cys Val Met Thr Gly Asn Val Ser Arg Cys Trp Val 225 230 235 240
- Gln Ile Thr Pro Thr Leu Ser Ala Pro Ser Leu Gly Ala Val Thr Ala 245 250 255
- Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala Gly Gly Ala Ala Leu Cys 260 265 270
- Ser Ala Leu Tyr Val Gly Asp Ala Cys Gly Ala Leu Phe Leu Val Gly 275 280 285
- Gln Met Phe Thr Tyr Arg Pro Arg Gln His Ala Thr Val Gln Asn Cys 290 295 300
- Asn Cys Ser Ile Tyr Ser Gly His Val Thr Gly His Arg Met Ala 305 310 315

121	INFORMATION	EC.2	SEO	TO	MO.	e = .
\ - /	INFORMALICA	FUR	350	111	MU:	J J .

- (1) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 354 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (11) MOLECULE TYPE: cDNA
- (111) HYPOTHETICAL: NO
- (111) ANTI-SENSE: NO
- (vii) IMMEDIATE SOURCE:

(B) CLONE: PC-1-37

- (1x) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..354
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 55:

ACCACCGGAG	CTTCTATCAC	ATACTCCACT	TACGGCAAGT	TCCTTGCTGA	TGGAGGGTGT	60
TCAGGCGGCG	CGCATGACGT	GATCATATGC	GACGAGTGCC	ATTCCCAGGA	CGCCACCACC	120
ATTCTTGGGA	TAGGCACTGT	CCTTGACCAG	GCAGAGACGG	CTGGAGCTAG	GCTCGTCGTC	180
TTGGCCACGG	NCACCCCTCC	CGGCAGTGTG	ACAACGCCCC	ACCCCAACAT	CGAGGAAGTG	240
GCCCTGCCTC	AGGAGGGGGA	GGTTCCCTTC	TACGGCAGAG	CCATTCCCCT	TGCTTTTATA	300
AAGGGTGGTA	GGCATCTCAT	CTTCTGCCAT	TCCAAGAAAA	ATTGTGATGA	ACTC	354

- (2) INFORMATION FOR SEQ ID NO: 56:
 - (1) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 118 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 56:

Thr Thr Gly Ala Ser Ile Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala 1 5 10 15

Asp Gly Gly Cys Ser Gly Gly Ala His Asp Val Ile Ile Cys Asp Glu 20 25 30

354

Суѕ	His	Ser 35	Gln	Asp	Ala	Thr	Thr 40	Ile	Leu	Gly	Ile	Gly 45	Thr	Val	Leu	
Asp	Gln 50	Ala	Glu	Thr	Ala	Gly 55	Ala	Arg	Leu	Val	Val 60	Leu	Ala	Thr	Xaa	
Th:= 65	Pro	Pro	Gly	Ser	Val 70	Thr	T'	Pro	His	Pro 75	Asn	Ile	Glu	Glu	Val 80	
Ala	Leu	Pro	Gln	Glu 85	Gly	Glu	Val	Pro	Phe 90	Tyr	Gly	Arg	Ala	Ile 95	Pro	
Leu	Ala	Phe	Ile 100	Lys	Gly	Gly	Arg	His 105	Leu	Ile	Phe	Cys	H1s	Ser	Lys	
Lys	Asn	Cys 115	qzA	Glu	Leu										_	
(2) INFOR	SEQU (A) (B) (C)	JENCE LEX TYP STE		ARACT : 354 nucle EDNES	TERIS La bas Blc a	STICS se pa acid sing!	S: airs									
(ii)	MOLE	CUL	E TY	PE: 0	ANCE											
(i1i)	HYPO	OTHE	FICAL	L: NO	3											
(iii)	ANT	-SE	NSE:	МО												
(vii)			TE SO ONE.													
(lx)	(A)	IAN	: ME/KI CATI(54										
(xi)	SEQ	JENC:	E DE	SCRI:	PTIO	N: S	EQ II	ON C	: 57	:						
ACCACCGG	AG C	TTCT.	ATCA	C AT	ACTO	CACT	TAC	GGCA	AGT '	TCCT	rgct	GA T	GGAG	GGTG	7	60
TCAGGCGG	eg e	GTAT(GACG'	r ga	TCAT	ATGC	GAC	gagt	GCC .	ATTC	CCAG	GA C	GCCA	CCAC	c	120
ATTCTTGG	GA T	AGGC.	ACTG'	r cc	TTGA	CCAG	GCA	GAGA	CGG	CTGG.	AGCT.	AG G	CTCG	TCGT	C	180
TTGGNCAC	GG N	CACC	CCTC	C CG	GCAG'	TGTG	ACA	ACGC	ccc	ACCC	CAAC	AT C	GAGG	aagt	G.	240
GCCCTGCC	TC A	GGAG	gggg.	A GG	TTCC	CTTC	TAC	GGNA	GAG	CCAT	TCCC	CT T	GCTT	TTAT	Ä.	300

- (2) INFORMATION FOR SEQ ID NO: 58:
 - (1) SEQUENCE CHARACTERISTICS:

AAGGGTGGTA GGCATCTCAT CTTCTGCCAT TCCAAGAAAA AATGTGATGA ACTT

- (A) LENGTH: 133 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 58:

Thr Thr Gly Ala Ser Ile Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala 1 5 10

Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Val Ile Ile Cys Asp Glu 20 25 30

Cys His Ser Gln Asp Ala Thr Thr Ile Leu Gly Ile Gly Thr Val Leu 35 40 45

Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val Leu Xaa Thr Xaa 50 55

Thr Pro Pro Gly Ser Val Thr Thr Pro His Pro Asn Ile Glu Glu Val 65 70 75 80

Ala Leu Pro Gln Glu Gly Glu Val Pro Phe Tyr Xaa Arg Ala Ile Pro 85 90 95

Leu Ala Phe Ile Lys Gly Gly Arg His Leu Ile Phe Cys His Ser Lys

Lys Lys Cys Asp Glu Leu Arg Gln Ala Thr Asp Gln Pro Gly Arg Glu 115 120 125

Arg Pro Trp Glu Tyr 130

- (2) INFORMATION FOR SEQ ID NO: 59:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 357 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: PC-1-37
 - (1x) FEATURE:
 - (A) NAME/KEY: CDS

(B) LOCATION: 1..357

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 59:

ATGGCTTTCA	TGTCTCCGGA	CTTGGAGGTC	ATTACCANCA	CTTGGGTTCT	GGTGGGGGC	60
GTTGTGGCGA	CCCTGNCGNC	CTACTGCTTG	ACGGTGGGTT	CGGTAGCCAT	AGTCGGTAGG	120
ATCATCCTCT	CTGGGAAACC	TGCCATCATT	NCCGATAGGG	AGGTATTATA	CCAGCAATTT	180
GATGAGATGG	AGGAGTGCTC	GGCCTCGTTG	CCCTATATGG	ACGAAACACG	TNCCATTGCC	240
GGACAATTCA	AAGAGAAAGT	GCTCGGCTTC	ATCAGCACGA	CCGGCCAGAA	GGCTGAAACT	300
CTGAAGCCGG	CAGCCACGTC	TGTGTGGAAC	AAGGCTGATC	AGTTCTGGNC	CACATAC	357

(2) INFORMATION FOR SEQ ID NO: 60:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 128 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (11) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 60:

Met Ala Phe Met Ser Pro Asp Leu Glu Val Ile Thr Xaa Thr Trp Val 1 5 10

Leu Val Gly Gly Val Val Ala Thr Leu Xaa Xaa Tyr Cys Leu Thr Val

Gly Ser Val Ala Ile Val Gly Arg Ile Ile Leu Ser Gly Lys Pro Ala 35 40 45

Ile Ile Xaa Asp Arg Glu Val Leu Tyr Gln Gln Phe Asp Glu Met Glu 50 55 60

Glu Cys Ser Ala Ser Leu Pro Tyr Met Asp Glu Thr Arg Xaa Ile Ala 65 70 75 83

Gly Gln Phe Lys Glu Lys Val Leu Gly Phe Ile Ser Thr Thr Gly Gln 85 90 95

Lys Ala Glu Thr Leu Lys Pro Ala Ala Thr Ser Val Trp Asn Lys Ala 100 105 110

Asp Gln Phe Trp Xaa Thr Tyr Met Trp Asn Phe Ile Ser Gly Ile Gln 115 120 125

(2) INFORMATION FOR SEQ ID NO: 61:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 357 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(11) MOLECULE TYPE: cDNA	
(111) HYPOTHETICAL: NO	
(111) ANTI-SENSE: NC	
(V11) IMMEDIATE SOURCE: (B) CLONE: PC-1-48	
(1x) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 1357	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 61:	
ATGGCTTGCA TGTCTGCGGA CCTGGAGGTC ATTACCANCA CTTGGGTTCT GGTGGGGGGC	60
TTGTGGGGN CCCTGGCGGC CTACTGCTTG ACGGTGGGTT CGGTAGCCAT AGTCGGTAGG	120
ATCATCOTOT CTGGGAAACO TGCCATCATT CCCGATAGGG AGGCATTATA CCANCAATTT	180
BATGAGATGG AGGAGTGCTC GGCCTCGTTG CCCTATATGG ACGAGACACG TGCCATTGCC 2	240
GACAATTCA AAGAGAAAGT GCTCGGCTTC ATCAGCACGA CCGGCCAGAA GGCTGAAACT	300
TGAAGCCGG CAGCCACGTC TGTGTGGAAC AAGGCTGANC AGTTCTGGGC CACATAC	357
(2) INFORMATION FOR SEQ ID NO: 62:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 128 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: protein	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 62:	
Met Ala Cys Met Ser Ala Asp Leu Glu Val Ile Thr Xaa Thr Trp Val 1 5 10 15	
Leu Val Gly Gly Val Val Ala Xaa Leu Ala Ala Tyr Cys Leu Thr Val 20 25 30	
Gly Ser Val Ala Ile Val Gly Arg Ile Ile Leu Ser Gly Lys Pro Ala 35 40 45	

50 55

Ile Ile Pro Asp Arg Glu Ala Leu Tyr Xaa Gln Phe Asp Glu Met Glu

Glu Cys Ser Ala Ser Leu Pro Tyr Met Asp Glu Thr Arg Ala Ile Ala 65 70 75 80

Gly Gln Phe Lys Glu Lys Val Leu Gly Phe Ile Ser Thr Thr Gly Gln 85 90 95

Lys Ala Glu Thr Leu Lys Pro Ala Ala Thr Ser Val Trp Asm Lys Ala 100 105 110

Xaa Gln Phe Trp Ala Thr Tyr Met Trp Asn Phe Ile Ser Gly Ile Gln
115 120 125

- (2) INFORMATION FOR SEQ ID NO: 63:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 28 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (111) HYPOTHETICAL: YES
 - (iii) ANTI-SENSE, NO
 - (1x) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION: 1..28
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCP:161"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 63:

ACCGGAGGCC AGGAGAGTGA TCTCCTCC

28

- (2) INFORMATION FOR SEQ ID NO: 64:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 28 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (1ii) HYPOTHETICAL: YES
 - (111) ANTI-SENSE. YES
 - (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION: 1..28
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr162"

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(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 64:	
GGGCTGCTCT ATCCTCATCG ACGCCATC	28
(2) INFORMATION FOR SEQ ID NO: 65:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 28 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(iii) HYPOTHETICAL: YES	
(iii) ANTI-SENSE: NO	
<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION: 128 (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr163"</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 65:	
GCCAGAGGCT CGGAAGGCGA TCAGCGCT	28
(2) INFORMATION FOR SEQ ID NO: 66:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 28 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(iii) HYPOTHETICAL: YES	
(iii) ANTI-SENSE: YES	
<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION: 128 (D) OTHER INFORMATION: /standard_name= "HCV Primer</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 66:	
GAGCTGCTCT GTCCTCCTCG ACGCCGCA	28
(2) INFORMATION FOR SEO ID NO: 67:	

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PCT/EP94/01323
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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 -
- (ii) MOLECULE TYPE: DNA (genomic)
- (iii) HYPOTHETICAL: YES
- (iii) ANTI-SENSE: NO
- (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION: 1..28
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr23"
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 67:

CTCATGGGGT ACATTCCGCT

20

- (2) INFORMATION FOR SEQ ID NO: 68:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 27 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: YES
 - (iii) ANTI-SENSE: YES
 - (ix) FEATURE:

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- (A) NAME/KEY: misc_feature
- (B) LOCATION: 1..28
- (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr54"
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 68:

CTATTACCAG TTCATCATCA TATCCCA

27

- (2) INFORMATION FOR SEQ ID NO: 69:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 24 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

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(iii) HYPOTHETICAL: YES

(iii) ANTI-SENSE: NO

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION: 1..28
- (D) OTHER INFORMATION: /standard_name= "HCV Primer
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 69:

TTTTAAATAC ATCATGRCTG YATG

24

- (2) INFORMATION FOR SEQ ID NO: 70:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 33 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: YES
 - (iii) ANTI-SENSE: YES
 - (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION: 1..28
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr66"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 70:

CTATTATTGT ATCCCRCTGA TGAARTTCCA CAT

33

- (2) INFORMATION FOR SEQ ID NO: 71:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 36 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: YES
 - (iii) ANTI-SENSE: YES
 - (ix) FEATURE:

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(A) NAME/KEY: misc_feature

- (B) LOCATION: 1..28
- (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPrll8:
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 71:

ACTAGTCGAC TAYTGATCCR CTATRWARTT CCACAT

36

- (2) INFORMATION FOR SEQ ID NO: 72:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 25 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: YES
 - (111) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION: 1..28
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HC2rll7:
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 72:

TTTTAAATAC ATCGCRCTGC ATGCA

25

- (2) INFORMATION FOR SEQ ID NO: 73:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 36 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: YES
 - (iii) ANTI-SENSE: YES
 - (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION: 1..28

 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 73:

ACTAGTCGAC TARTTGCATA GCCKRTTCAT CCAYTG

36

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(2) INFORMATION FOR SEQ ID NO: 74:

(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 34 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(iii) HYPOTHETICAL: YES	
(ili) ANTI-SENSE: NO	
<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION: 128 (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr131:</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 74:	
GGAATTCTAG ACCTCTGGGA YGARAYTGGA ARTG	34
(2) INFORMATION FOR SEQ ID NO: 75:	
(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 31 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(iii) HYPOTHETICAL: YES	
(iii) ANTI-SENSE: NO	
<pre>(1x) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION: 128 (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr130:</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 75:	
GGAATTCTAG ACGCTAYCAR GCACGTTGYG C	31
(2) INFORMATION FOR SEQ ID NO: 76:	,
(1) SEQUENCE CHARACTERISTICS:(A) LENGTH: 23 base pairs(B) TYPE: nucleic acid	

157

(C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(iii) HYPOTHETICAL: YES	
(iii) ANTI-SENSE: NO	
(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION: 128 (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr134: (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 76: CATATAGATG CCCACTTCCT ATC (2) INFORMATION FOR SEQ ID NO: 77: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	23
(ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: YES	
(iii) ANTI-SENSE: YES	
<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION: 128 (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr3:</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 77: GTGTGCCAGG ACCATC	16
(2) INFORMATION FOR SEQ ID NO: 78:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	

(ii) MOLECULE TYPE: DNA (genomic)

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(iii) HYPOTHETICAL: YES

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(iii) ANTI-SENSE: YES
  (ix) FEATURE:
          (A) NAME/KEY: misc_feature
          (B) LOCATION: 1..28
          (D) OTHER INFORMATION: /standard_name= "HCV Primer
    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 78:
GACATGCATG TCATGATGTA
                                                                        20
(2) INFORMATION FOR SEQ ID NO: 79:
     (i) SEQUENCE CHARACTERISTICS:
          (A) LENGTH: 29 base pairs
          (B) TYPE: nucleic acid
          (C) STRANDEDNESS: single
          (D) TOPOLOGY: linear
    (ii) MOLECULE TYPE: DNA (genomic)
   (iii) HYPOTHETICAL: NO
   (iii) ANTI-SENSE: NO
  (1x) FEATURE:
          (A) NAME/KEY: misc_feature
          (B) LOCATION: 1..28
          (D) OTHER INFORMATION: /standard_name= "HCV Primer
                 HCPr152:
    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 79:
TACGCCTCTT CTATATCGGT TGGGGCCTG
                                                                        29
(2) INFORMATION FOR SEQ ID NO: 80:
     (i) SEQUENCE CHARACTERISTICS:
          (A) LENGTH: 26 base pairs
          (B) TYPE: nucleic acid
          (C) STRANDEDNESS: single
          (D) TOPOLOGY: linear
    (ii) MOLECULE TYPE: DNA (genomic)
   (iii) HYPOTHETICAL: YES
   (iii) ANTI-SENSE: NO
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- - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr52:
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 80:

ATGTTGGGTA AGGTCATCGA TACCCT

25

- (2) INFORMATION FOR SEQ ID NO: 81:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 25 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: YES
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: misc feature
 - (B) LOCATION: 1..28

 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 81:

CCCGGGAGGT CTCGTAGACC GTGCA

25

- (2) INFORMATION FOR SEQ ID NO: 82:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 29 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: YES
 - (iii) ANTI-SENSE: YES
 - (ix) FEATURE:

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- (A) NAME/KEY: misc_feature
- (B) LOCATION: 1..28
- (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr40:

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 82:

CTATTAAAGA TAGAGAAAGA GCAACCGGG

29

- (I) INFORMATION FOR SEQ ID NO: 83:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 12 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (viii) POSITION IN PROTEIN:
- (B) MAP POSITION: positions 192 to 203 of the V1 region of HCV

type 3

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- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 83: Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu
- (2) INFORMATION FOR SEQ ID NO: 84:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 12 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (viii) POSITION IN PROTEIN:
- (B) MAP POSITION: positions 192 to 203 of the V1 region of HCV type 5
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 84:

Val Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val

- (2) INFORMATION FOR SEQ ID NO: 85:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 11 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single

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- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (viii) POSITION IN PROTEIN:
- (B) MAP POSITION: positions 213 to 223 of the V2 region of HCV type 3
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 85:

Val Tyr Glu Ala Asp Asp Val Ile Leu His Thr

- (2) INFORMATION FOR SEQ ID NO: 86:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 11 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
- - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 86:

Val Tyr Glu Ala Asp Asn Leu Ile Leu His Ala 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 87:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 13 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO

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162

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 87: Val Gln Asp Gly Asn Thr Ser Thr Cys Trp Thr Pro Val 10 (2) INFORMATION FOR SEQ ID NO: 88: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 13 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: single (D) TOPCLOGY: linear (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (viii) POSITION IN PROTEIN: (B) MAP POSITION: positions 230 to 242 of the V3 region of HCV type 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 88: Val Met Thr Gly Asn Val Ser Arg Cys Trp Val Gln Ile (2) INFORMATION FOR SEQ ID NO: 89: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 10 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (viii) POSITION IN PROTEIN: (B) MAP POSITION: positions 248 to 257 of the V4 region of HCV type 3 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 89: Val Arg Tyr Val Gly Ala Thr Thr Ala Ser 5 (2) INFORMATION FOR SEQ ID NO: 90: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 10 amino acids (B) TYPE: amino acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (viii) POSITION IN PROTEIN:

(B) MAP FOSITION: positions 248 to 257 of the V4 region of HCV type 5 $\,$

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 90:

Ala Pro Ser Leu Gly Ala Val Thr Ala Pro 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 91:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (viii) POSITION IN PROTEIN:

(B) MAP POSITION: positions 294 to 303 of the V5 region of HCV type 3 $\,$

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 91:

Arg Pro Arg Arg His Gln Thr Val Gln Thr 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 92:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (viii) POSITION IN PROTEIN:
- (B) MAP POSITION: positions 294 to 303 of the V5 region of HCV type 5 $\,$

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 92:

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Arg Pro Arg Gln His Ala Thr Val Gln Asn
(2) INFORMATION FOR SEQ ID NO: 93:
     (i) SEQUENCE CHARACTERISTICS:
         (A) LENGTH: 9 amino acids
         (B) TYPE: amino acid
         (C) STRANDEDNESS: single
         (D) TOPOLOGY: linear
   (ii) MOLECULE TYPE: peptide
  (iii) HYPOTHETICAL: NO
  (viii) POSITION IN PROTEIN:
          (B) MAP POSITION: positions 70 to 78 of HCV type 5
    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 93:
    Gln Pro Thr Gly Arg Ser Trp Gly Gln
(2) INFORMATION FOR SEQ ID NO: 94:
     (i) SEQUENCE CHARACTERISTICS:
          (A) LENGTH: 8 amino acids
          (B) TYPE: amino acid
          (C) STRANDEDNESS: single
          (D) TOPOLOGY: linear
    (ii) MOLECULE TYPE: peptide
   (iii) HYPOTHETICAL: NO
    (vi) ORIGINAL SOURCE:
         (C) INDIVIDUAL ISOLATE: BR33 and BR36
  (viii) POSITION IN PROTEIN:
         (B) MAP POSITION: positions 230 to 237 of the V3 region of HCV
type 3
    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 94:
     Val Gln Asp Gly Asn Thr Ser Thr
(2) INFORMATION FOR SEQ ID NO: 95:
     (i) SEQUENCE CHARACTERISTICS:
          (A) LENGTH: 8 amino acids
          (B) TYPE: amino acid
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(C) STRANDEDNESS: single

- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISCLATE: HD10
- (viii) POSITION IN PROTEIN:
- (B) MAP POSITION: positions 230 to 237 of the V3 region of HCV type 3
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 95:

Val Gln Asp Gly Asn Thr Ser Ala

- (2) INFORMATION FOR SEQ ID NO: 96:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: BR36
 - (viii) POSITION IN PROTEIN:
 - (B) MAP POSITION: positions 248 to 257 of the V4 region of HCV
- type 3

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 96:

Val Lys Tyr Val Gly Ala Thr Thr Ala Ser

- (2) INFORMATION FOR SEQ ID NO: 97:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: BR36

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(viii) POSITION IN GENOME:
          (B) MAP POSITION: Positions 1688 to 1707 of HCV type 3
    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 97:
     Leu Gly Gly Lys Pro Ala Ile Val Pro Asp Lys Glu Val Leu Tyr Gln
     Gln Tyr Asp Glu
                20
(2) INFORMATION FOR SEQ ID NO: 98:
     (i) SEQUENCE CHARACTERISTICS:
          (A) LENGTH: 20 amino acids
          (B) TYPE: amino acid
          (C) STRANDEDNESS: single
          (D) TOPOLOGY: linear
    (ii) MOLECULE TYPE: peptide
   (iii) HYPOTHETICAL: NO
    (vi) ORIGINAL SOURCE:
         (C) INDIVIDUAL ISOLATE: HD10
  (viii) POSITION IN GENOME:
          (B) MAP POSITION: positions 1688 to 1707 of HCV type 3
    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 98:
    Leu Gly Gly Lys Pro Ala Leu Val Pro Asp Lys Glu Val Leu Tyr Gln
                                       10
    Gln Tyr Asp Glu
(2) INFORMATION FOR SEQ ID NO: 99:
    (i) SEQUENCE CHARACTERISTICS:
         (A) LENGTH: 20 amino acids
         (B) TYPE: amino acid
         (C) STRANDEDNESS: single
         (D) TOPOLOGY: linear
   (ii) MOLECULE TYPE: peptide
  (iii) HYPOTHETICAL: NO
 (viii) POSITION IN GENOME:
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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 99:

(B) MAP POSITION: positions 1712 to 1731

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Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala His Gln 1 5 10 15

Phe Lys Glu Lys 20

- (2) INFORMATION FOR SEQ ID NO: 100:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: BR36
 - (viii) POSITION IN GENOME:
 - (B) MAP POSITION: positions 1724 to 1743 of HCV type 3
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 100:

Ile Ala His Gln Phe Lys Glu Lys Val Leu Gly Leu Leu Gln Arg Ala 1 5 10 15

Thr Gln Gln Gln

- (2) INFORMATION FOR SEQ ID NO: 101:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: HD10
 - (viii) POSITION IN GENOME:
 - (B) MAP POSITION: positions 1724 to 1743 of HCV type 3
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 101:

Ile Ala His Gln Phe Lys Glu Lys Ile Leu Gly Leu Leu Gln Arg Ala 1 5 10 15

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Thr Gln Gln Gln
   20
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- (2) INFORMATION FOR SEQ ID NO: 102:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (viii) POSITION IN GENOME:
 - (B) MAP POSITION: positions 1688 to 1707 of HCV type 5
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 102:

Leu Ser Gly Lys Pro Ala Ile Ile Pro Asp Arg Glu Ala Leu Tyr Gln 10 15 .

Gln Phe Asp Glu

20

- (2) INFORMATION FOR SEQ ID NO: 103:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (viii) POSITION IN GENOME:
 - (B) MAP POSITION: positions 1688 to 1707
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 103:

Leu Ser Gly Lys Pro Ala Ile Ile Pro Asp Arg Glu Val Leu Tyr Gln 10

Gln Phe Asp Glu

- (2) INFORMATION FOR SEQ ID NO: 104:
 - (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 amino acids

- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (111) HYPOTHETICAL: NO
- (viii) POSITION IN GENOME:
 - (B) MAP POSITION: position 1712 to 1731 of HCV type 5
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 104:

Ser Ala Ser Leu Pro Tyr Met Asp Glu Thr Arg Ala Ile Ala Gly Gln
1 5 10 15

Phe Lys Glu Lys 20

- (2) INFORMATION FOR SEQ ID NO: 105:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (viii) POSITION IN GENOME:
 - (B) MAP POSITION: positions 1724 to 1743 of HCV type 5
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 105:

Ile Ala Gly Gln Phe Lys Glu Lys Val Leu Gly Phe Ile Ser Thr Thr 1 5 10 15

Gly Gln Lys Ala

- (2) INFORMATION FOR SEQ ID NO: 106:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 340 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO

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(III) ANII-SENSE: NO	(iii)	ANTI-SENSE:	NO
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(vii) IMMEDIATE SOURCE:

(B) CLONE: GB48-3-10

(1x) FEATURE:

(A) NAME/KEY: CDS
(B) LOCATION: 2..340

(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 106:

		GAG GAG GAG GTC TAT Glu Glu Glu Val Tyr 15	46
		G GCA ATT ACC GCC CT 'S Ala Ile Thr Ala Le 30	
Thr Glu Arg Le		T AAC AGC AAG GGA GA s Ast Ser Lys Gly As 45	
		C GTC TAC ACC ACC AG y Val Tyr Thr Thr Se 60	
		C TCA GCC GCT ATC AA a Ser Ala Ala Ile Ly 75	
	Thr Met Leu Va	TC TGT GGT GAT GAC CT Li Cys Gly Asp Asp Le 90	
		AG GAC AAA CGA CCC CT .u Asp Lys Arg Pro Le 110	
GGA GCC Gly Ala			340

(2) INFORMATION FOR SEQ ID NO: 107:

- (1) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE. protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 107:

Ser Thr Val Thr Glu Lys Asp Ile Arg Val Glu Glu Glu Val Tyr Gln
1 5 10 15

Суз	Суз	Asp	Leu 20	Glu	Pro	Glu	Ala	Arg 25	Lys	Ala	Ile	Thr	Ala 30	Leu	Thr		
Glu	Arg	Leu 35	Tyr	Val	Gly	Gly	Pro 40	Met	His	Asn	Ser	Lys 45	Gly	Asp	Leu		
CÀ2	Gly 50	Tyr	Arg	Arg	Civa	Arg 55	Ala	Ser	Gly	Val	Ty: 60	Thr	Thr	Ser	Phe		
Gly 65	Asn	Thr	Leu	Thr	Cys 70	Tyr	Leu	Lys	Ala	Ser 75	Ala	Ala	Ile	Lys	Ala 80		
Ala	Gly	Leu	Arg	Asp 85	Cys	Thr	Met	Leu	Val 90	Cys	Gly	Asp	ÇZA	Leu 95	Val		
Val	Ile	Ala	Glu 100	Ser	Asp	Gly	Val	Glu 105	Glu	Asp	Lys	Arg	Pro 110	Leu	Gly	-	
Ala																	
(2)	INF	ORMA:	TION	FOR	SEQ	ID 1	NO:	108:									
	(ii (iii (lii (vii (ix	(;; (;; (;; (;; (;; (;; (;; (;; (;; (;;	A) L: B) T' C) S' C) S' LECU POTH TI-S MEDI B) C ATUR A) N B) L	ENGTT YPE: TRANN OPOL LE T ETIC ENSE ATE LONE E: AME/ OCAT	H: 3 nuc DEDN OGY: YPE: AL: : NO SOUR : GB		acr sin ear A	pair d gle		IO: 1	OB.						
CI	(XI CC A	•	•									GAG (GAG (GTA T	TAT		46
S	er T	hr V	al T	hr G	lu I 5	.ys A	rab I	le A	urg V	/al 6	Slu (Glu (Glu V	Jal 1	Tyr 15		
					ı Glu					arg					CTA a Leu		94
															A GAC y A sp		142

3.5

40 45

CTG Leu	TGC Cys	GGG Gly 50	TAT Tyr	CGC Arg	AGA Arg	TGC Cys	CGT Arg 55	GCG Ala	AGC Ser	GGC Gly	GTC Val	TAC Tyr 60	ACC Thr	ACC Thr	AGC Ser	190
TTC Phe	GGG Gly 65	AAC Asn	ACA Thr	CTG Leu	ACG Thr	TGC Cys 70	TAT Tyr	CTC Leu	AAA Lys	GCC Ala	TCA Ser 75	GCC Ala	GCT Ala	ATC Ile	AGA Arg	238
GCG Ala 80	GCG Ala	GGG Gly	CTG Leu	AGA Arg	GAC Asp 85	TGC Cys	ACC Thr	ATG Met	TTG Leu	GTC Val 90	TGT Cys	GGT Gly	GAT Asp	GAC Asp	CTG Leu 95	286
GTC Val	GTC Val	ATT Ile	GCT Ala	GAA Glu 100	AGC Ser	GAT Asp	GGC Gly	GTA Val	GAG Glu 105	GAG Glu	GAC Asp	AAA Lys	CGA Arg	GCC Ala 110	CTC Leu	334
GGA Gly																340

(2) INFORMATION FOR SEQ ID NO: 109:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:

Ser Thr Val Thr Glu Lys Asp Ile Arg Val Glu Glu Glu Val Tyr Gln
1 5 10 15

Cys Cys Asp Leu Glu Pro Glu Ala Arg Arg Ala Ile Thr Ala Leu Thr 20 $$\rm 25$$ 30

Glu Arg Leu Tyr Val Gly Gly Pro Met His Asn Ser Arg Gly Asp Leu
35 40

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Phe 50 55 60

Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Ile Arg Ala 65 70 75 80

Ala Gly Leu Arg Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu.Val
85 90 95

Val Ile Ala Glu Ser Asp Gly Val Glu Glu Asp Lys Arg Ala Leu Gly
100 105 110

Ala

(2) INFORMATION FOR SEQ ID NO: 110:

- (1) SEQUENCE CHARACTERISTICS:(A) LENGTH: 340 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (111) HYPOTHETICAL: NO
- (iii) ANTI-SENSE: NO
- (vii) IMMEDIATE SOURCE:
 - (B) CLONE: GB215-3-8
- (ix) FEATURE:
 - (A) NAME/KEY: CDS
 (B) LOCATION: 2..340
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 110:

	CC GAA AAA GAC A nr Glu Lys Asp I 5			46
			A ATT ACC GCC CTA l Ile Thr Ala Leu 30	94
			T AGC AAA GGA GAC n Ser Lys Gly Asp 45	142
		Ala Ser Gly Val	C TAC ACC ACC AGC 1 Tyr Thr Thr Ser 60	190
			A GCC GCC ATC AGG r Ala Ala Ile Arg 5	238
			T GGT GAC GAC CTG r Gly Asp Asp Leu 95	286
			C AAA CGA GEC CTC p Lys Arg Ala Leu 110	334
GGA GTC Gly Val				340

(2) INFORMATION FOR SEQ ID NO: 111:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 111:

Ser Thr Val Thr Glu Lys Asp Ile Arg Val Glu Glu Glu Val Tyr Gln 10

Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Thr Ala Leu Thr 20 25

Glu Arg Leu Tyr Val Gly Gly Pro Met His Asn Ser Lys Gly Asp Leu

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Phe 55

Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Ile Arg Ala 70

Ser Gly Leu Arg Asp Cys Thr Met Leu Val Tyr Gly Asp Asp Leu Val 85

Val Ile Ala Glu Ser Asp Gly Val Glu Glu Asp Lys Arg Ala Leu Gly 100 105

Val

- (2) INFORMATION FOR SEQ ID NO: 112:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 340 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: GB358-3-3
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 2..340
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 112:
- C TCC ACT GTA ACC GAA AAG GAC ATC AGG GTC GAG GAG GAG GTG TAT 46

Se	er Th	ır Va	al Th	ır Gl	.ս Lչ 5	/s As	sp Il	.e Ar	1 G1 .0	u Gl	u Gl	.u Va	r .5	
			GAC Asp											94
			CTC Leu 35										GAC Asp	142
			TAT Tyr											190
													AGA Arg	238
													CTG Leu 95	286
					Ser				Glu				CTC Leu	
	GCC Ala													340

(2) INFORMATION FOR SEQ ID NO: 113:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 113:

Ser Thr Val Thr Glu Lys Asp Ile Arg Val Glu Glu Glu Val Tyr Gln

Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Ala Ile Thr Ala Leu Thr 20 25 30 .

Glu Arg Leu Tyr Val Gly Gly Pro Met His Asn Ser Lys Gly Asp Leu 35 40 45

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Phe 50 55 60

Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Ile Arg Ala 65 70 75 80

1/6	
Ala Gly Leu Arg Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val 85 90 95	
Val Ile Ala Glu Ser Asp Gly Val Glu Glu Asp Lys Arg Ala Leu Gly 100 105 110	
Ala	
(2) INFORMATION FOR SEQ ID NO: 114:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 340 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: cDNA	
(iii) HYPOTHETICAL: NO	
(iii) ANTI-SENSE: NO	
(vii) IMMEDIATE SOURCE: (B) CLONE: GB549-3-6	
(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 2340	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 114:	_
C TCC ACG GTG ACC GAA AGG GAT ATC AGG ACC GAG GAA GAG ATC TAC Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Glu Ile Tyr 1 5 10 15	4.5
CAG TGC TGC GAC CTG GAG CCC GAA GCC CGC AAG GTG ATA TCC GCC CTA Gln Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Ser Ala Leu 20 25 30	94
ACG GAA AGA CTC TAC GTG GGC GGT CCC ATG TAC AAC TCC AAG GGG GAC Thr Glu Arg Leu Tyr Val Gly Gly Pro Met Tyr Asn Ser Lys Gly Asp 35 40 45	142
CTA TGC GGG CAA CGG AGG TGC CGC GCA AGC GGG GTC TAC ACC ACC AGC Leu Cys Gly Gln Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser 50 60	190
TTC GGG AAC ACT GTA ACG TGT TAT CTC AAG GCC GTT GCG GCT ACT AGG Phe Gly Asn Thr Val Thr Cys Tyr Leu Lys Ala Val Ala Ala Thr Arg 65 70 75	238
GCC GCA GGT CTG AAA GGT TGC AGC ATG CTG GTT TGT GGA GAC GAC TTA	286

Ala Ala Gly Leu Lys Gly Cys Ser Met Leu Val Cys Gly Asp Asp Leu

90

85

GTC GTC ATC TGC GAG AGC GGC GGC GTA GAG GAG GAT GCA AGA GCC CTC

Val Val Ile Cys Glu Ser Gly Gly Val Glu Glu Asp Ala Arg Ala Leu

100 105 110

CGA GCC Arg Ala 340

- (2) INFORMATION FOR SEQ ID NO: 115:
 - (1) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 115:

Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Glu Ile Tyr Gin
1 5 10 15

Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Ser Ala Leu Thr 20 25 30

Glu Arg Leu Tyr Val Gly Gly Pro Met Tyr Asn Ser Lys Gly Asp Leu 35 40 45

Cys Gly Gln Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Phe

Gly Asn Thr Val Thr Cys Tyr Leu Lys Ala Val Ala Ala Thr Arg Ala 65 70 75 80

Ala Gly Leu Lys Gly Cys Ser Met Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Val Ile Cys Glu Ser Gly Gly Val Glu Glu Asp Ala Arg Ala Leu Arg 100 105 110

Ala

- (2) INFORMATION FOR SEQ ID NO: 116:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 340 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (11) MOLECULE TYPE: cDNA
 - (111) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO

i	(vil)		MEDIA 3) CI				3-1									
	(ix)	(2	ATURI A) NU B) LO	AME/I			340									
	(xi)	SE	QUENC	E DE	ESCR	EPTIC	N: 5	EQ :	D NO): 11	L6 :					
	TCC ACT GTG ACT GAG AGA GAC ATC AAG GTC GAA GAA GAA GTC TAT Ser Thr Val Thr Glu Arg Asp Ile Lys Val Glu Glu Glu Val Tyr 1 5 10 15 AG TGT TGT GAT CTG GAG CCC GAG GCC CGC AAG GTA ATA GCC GCC CTC ln Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Ala Ala Leu															46
																94
			CTC Leu 35													142
			TAT													190
			ACA Thr													238
			CTA Leu													286
			GCC Ala													334
	GCT Ala															340
(2)	INF		TION SEOU													
		(A) L B) T D) T	ENGT YPE :	H: 1 ami	13 a no a	mino cid									
	(ii) MO	LECU	LE T	YPE:	pro	tein	ı								

Ser Thr Val Thr Glu Arg Asp Ile Lys Val Glu Glu Glu Val Tyr Gln

(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 117:

Cys Cys Asp Leu Glu P	o Glu Ala Arg Lys Val	Ile Ala Ala Leu Thr
20	25	30

Glu Arg Leu Tyr Val Gly Gly Pro Met His Asn Ser Lys Gly Asp Leu 35 40 45

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Phe 50 55 60

Gly Asn Thr Met Thr Cys Tyr Leu Lys Ala Ser Ala Ala Ile Arg Ala 65 70 75 80

Ala Gly Leu Lys Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val
85 90 95

Val Ile Ala Glu Ser Gly Gly Val Glu Glu Asp Lys Arg Ala Leu Gly
100 105 110

Ala

(2) INFORMATION FOR SEQ ID NO: 118:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 574 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: NO
- (111) ANTI-SENSE: NO
- (vii) IMMEDIATE SOURCE:
 - (B) CLONE: GB358-4-1
- (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..574
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 118:

ACT TGC GGC TTT GCC GAC CTC ATG GGA TAC ATC CCG CTC GTA GGC GCC

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala

1 5 10 15

CCT GTG GGT GGC GCC AGG GCC CTG GCA CAC GGT GTT AGG GCT GTG 96
Pro Val Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val
20 25 30

GAG GAC GGG ATC AAT TAT GCG ACA GGG AAT CTT CCC GGT TGC TCT TTC
Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe

35
40
45

TCT Ser	ATC Ile 50	TTC Phe	CTC Leu	TTG Leu	GCA Ala	CTT Leu 55	CTT Leu	TCG Ser	TGC Cys	CTG Leu	ACT Thr 60	GTT Val	CCC Pro	ACC Thr	TCG Ser		192
GCC Ala 65	GTC Val	AAC Asn	TAT Tyr	CGC Arg	AAT Asn 70	GCC Ala	TCG Ser	GGC Gly	ATC Ile	TAT Tyr 75	CAC His	ATC Ile	ACC Thr	AAT Asn	GAC Asp 80		240
TGC Cys	CCG Pro	AAC Asn	TCG Ser	AGC Ser 85	ATA Ile	GTG Val	TAC Tyr	GAG Glu	ACC Thr 90	GAG Glu	CAC His	CAC His	ATC Ile	CTA Leu 95	CAC H1s		288
CTC Leu	CCA Pro	GGG Gly	TGT Cys 100	TTA Leu	bro CCC	TGC Cys	GTG Val	AGG Arg 105	GTT Val	GGG Gly	AAT Asn	CAG Gln	TCA Ser 110	CGC Arg	TGC Cys		336
TGG Trp	GTG Val	GCC Ala 115	CTC Leu	ACT Thr	CCC Pro	ACC Thr	GTG Val 120	GCG Ala	GCG Ala	CCT Pro	TAC Tyr	ATC Ile 125	GGC Gly	GCT Ala	CCG Pro	-	384
														GCT Ala			432
														TTC Phe			480
														ACG Thr 175			528
			TGT Cys 180											AGG Arg	A		574

(2) INFORMATION FOR SEQ ID NO: 119:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 191 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 119:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala 1 5 10

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Thr Ser

181 Ala Val Asn Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile Thr Asn Asp 70 Cys Pro Asn Ser Ser Ile Val Tyr Glu Thr Glu His His Ile Leu His Leu Pro Gly Cys Leu Pro Cys Val Arg Val Gly Asn Gln Ser Arg Cys Trp Val Ala Leu Thr Pro Thr Val Ala Ala Pro Tyr Ile Gly Ala Pro Leu Glu Ser Leu Arg Ser His Val Asp Leu Met Val Gly Ala Ala Thr Ala Cys Ser Ala Leu Tyr Ile Gly Asp Leu Cys Gly Gly Val Phe Leu Val Gly Gln Met Phe Ser Phe Gln Pro Arg Arg His Trp Thr Thr Gln 170 Asp Cys Asn Cys Ser Ile Tyr Ala Gly His Val Thr Gly His Arg 185 (2) INFORMATION FOR SEQ ID NO: 120: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 574 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: cDNA (iii) HYPOTHETICAL: NO (iii) ANTI-SENSE: NO (vii) IMMEDIATE SOURCE: (B) CLONE: GB549-4-3 (ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 1..574 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 120:

ACG TGC GGC TTT GCC GAC CTC ATG GGA TAC ATC CCG CTC GTG GGC GCC

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala

1 5 10 15

CCT GTG GGT GGC GTC GCC AGG GCC TTG GCA CAT GGT GTC AGG GCC GTG

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val

20 25 30

GAG Glu	GAC Asp	GGG Gly 35	ATT Ile	AAC Asn	TAT Tyr	GCA Ala	ACA Thr 40	GGG Gly	AAT Asn	CTT Leu	CCC Pro	GGT Gly 45	TGC Cys	TCC Ser	TTT Phe		144
TCT Ser	ATC Ile 50	TTC Phe	CTT Leu	CTA Leu	GCA Ala	CTT Leu 55	CTC Leu	TCG Ser	TGC Cys	TTG Leu	ACT Thr 60	GTC Val	CCG Pro	GCC Ala	TCG Ser		192
GCG Ala 65	CAG Gln	CAC His	TAC Tyr	CGG Arg	AAC Asn 70	ATC Ile	TCG Ser	GGC Gly	ATT Ile	TAT Tyr 75	CAC His	GTC Val	ACC Thr	AAT Asn	GAC Asp 80		240
TGC Cys	CCG Pro	AAC Asn	TCT Ser	AGT Ser 85	ATA Ile	GTG Val	TAT Tyr	GAA Glu	GCT Ala 90	GAC Asp	CAT His	CAT His	ATC Ile	ATG Met 95	CAT His		288
					CCT Pro											-	336
					CCC Pro												384
					CGG Arg												432
					TAC Tyr 150												480
					ACC Thr												528
					ATC Ile										A		574

(2) INFORMATION FOR SEQ ID NO: 121:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 191 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 121:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala
1 10 15

Pro Val Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val 20 25 30

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55 60

Ala Gln His Tyr Arg Asn Ile Ser Gly Ile Tyr His Val Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp His His Ile Met His 85 90 95

Leu Pro Gly Cys Val Pro Cys Val Arg Thr Gly Asn Thr Ser Arg Cys
100 105 110

Trp Val Pro Leu Thr Pro Thr Val Ala Pro Tyr Val Gly Ala Pro 115 120 125

Leu Glu Ser Met Arg Arg His Val Asp Leu Met Val Gly Ala Ala Thr 130 135 140

Val Cys Ser Ala Leu Tyr Ile Gly Asp Leu Cys Gly Gly Val Phe Leu 145 150 155 160

Val Gly Gln Mec Phe Thr Phe Arg Pro Arg Arg His Trp Thr Thr Gln 165 170 175

Asp Cys Asn Cys Ser Ile Tyr Asp Gly His Ile Thr Gly His Arg 180 185 190

- (2) INFORMATION FOR SEQ ID NO: 122:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 574 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: GB809-4-3
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..574
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 122:

ACG TGC GGC TTC GCC GAC CTC ATG GGA TAC ATC CCG CTC GTG GGC GCC

	CÀ2	Gly	Phe	_	Asp	Leu	Met	Gly		Ile	Pro	Leu	Val	•	Ala		
1				5					10					15			
~~~	تتبت	ccc	GGC	GTC.	ecc	) CC	GCC	حسرت	ece	CZT	ccc		NCC.	~~ <del>~</del>	C#C		0.0
			Gly														96
		011	20					25			G. J.	V CA 1	30	AL. 0	V (A _		
													3.0				
GAG	GAC	GGG	ATT	AAC	TAT	GCG	ACA	GGG	AAT	CTT	CCC	GGT	TGC	TCT	TTC		144
Glu	Asp	Gly	Ile	Asn	Tyr	Ala	Thr	Gly	Asn	Leu	Pro	Gly	Cys	Ser	Phe		
		35					40					45					
			CTC														192
Ser		Phe	Leu	Leu	ALA		Leu	Ser	cys	Leu		val	Pro	Ala	Ser		
	50					<b>5</b> 5					60						
GCT	GAG	CAC	TAC	CGG	AAT	GCT	TCG	GGC	ATC	TAT	CAC	ATC	ACC	TAG	GAC		240
			Tyr														
65				,	70					75					80	-	
			TCC														288
Cys	Pro	Asn	Ser	Ser	Va:	Val	Tyr	Glu	Thr	Asp	Hls	Hls	Ile	Leu	Hıs		
				85					90					95			
mma					~~~	<b></b>			404								
			TGC														336
Leu	Pro	GIY	Cys 100	Vai	PIG	CAR	vai	105	міа	GTÀ	ASI	vai	ser 110	Arg	Cys		
TGG	ACG	COG		aca	CCT	ACG	GTG		GCC	Gm2	TCC	ATG		GCT	CCG		384
			Val														301
		115					120					125					
CTC	GAG	TCC	TTC	CGG	CGG	CAT	GTG	GAC	CTA	ATG	GTA	GGT	GCG	GCC	ACC		432
Leu	Glu	Ser	Phe	Arg	Arg	äıs	Val	qzA	Leu	Met	Val	Glγ	Ala	Ala	Thr		
	130					135					140						
															CTA		480
145	-	ser	Val	rea	150	Val	GIY	ASD	Leu	155	-	GTĀ	ALA	Pue	Leu 160		
7.4.3					0					*72					100		•
GTG	GGG	CAG	ATG	TTC	ACC	TTC	CAG	CCG	CGT	CGC	CAC	TGG	ACC	ACG	CAG		528
															Gln		
	•			165					170	-		•		175			
			TGC														574
Asp	Cys	Asn	Cys		Ile	Tyr	Thr	-		Ile	Thr	Gly		_			
			180					183	5				190				

# (2) INFORMATION FOR SEQ ID NO: 123:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 191 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (11) MOLECULE TYPE: protein
- (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 123:

- Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala
  1 5 10 15
- Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val 20 25 30
- Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45
- Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55 60
- Ala Glu His Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile Thr Asn Asp 65 70 75 80
- Cys Pro Asn Ser Ser Val Val Tyr Glu Thr Asp His His Ile Leu His
  85 90 95
- Leu Pro Gly Cys Val Pro Cys Val Arg Ala Gly Asn Val Ser Arg Cys
  100 105 110
- Trp Thr Pro Val Thr Pro Thr Val Ala Ala Val Ser Met Asp Ala Pro 115 120 125
- Leu Glu Ser Phe Arg Arg His Val Asp Leu Met Val Gly Ala Ala Thr 130 135 140
- Val Cys Ser Val Leu Tyr Val Gly Asp Leu Cys Gly Gly Ala Phe Leu 145 150 155 160
- Val Gly Gln Met Phe Thr Phe Gln Pro Arg Arg His Trp Thr Thr Gln 165 170 175
- Asp Cys Asn Cys Ser Ile Tyr Thr Gly His Ile Thr Gly His Arg 180 185 190
- (2) INFORMATION FOR SEQ ID NO: 124:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 31 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: DNA (genomic)
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: NO
  - (1x) FEATURE:
    - (A) NAME/KEY: misc_feature
    - (B) LOCATION: 1..31
    - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr206"
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 124:

# 186 TGGGGATCCC GTATGATACC CGCTGCTTTG A 31 (2) INFORMATION FOR SEQ ID NO: 125: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO (iii) ANTI-SENSE: YES (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION: 1..30 (D) OTHER INFORMATION: /standard_name= "HCV Primer HcPr207" (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 125: GGCGGAATTC CTGGTCATAG CCTCCGTGAA 30 (2) INFORMATION FOR SEQ ID NO: 126: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 12 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (vi) ORIGINAL SOURCE: (A) ORGANISM: amino acid (C) INDIVIDUAL ISOLATE: GB358 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 126: Val Asn Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile (2) INFORMATION FOR SEQ ID NO: 127: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 12 amino acids

- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide

- (iii) HYPOTHETICAL: NO
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Amino acid
  - (C) INDIVIDUAL ISOLATE: GB549
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 127:

Gln His Tyr Arg Asm Ile Ser Gly Ile Tyr His Val

- (2) INFORMATION FOR SEQ ID NO: 128:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 12 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (11) MOLECULE TYPE: peptide
  - (111) HYPOTHETICAL: NO
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Amino acid
    - (C) INDIVIDUAL ISOLATE: GB809
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 128:

Glu His Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 129:
  - (1) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 11 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (iii) HYPOTHETICAL: NO
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: amino acid
    - (C) INDIVIDUAL ISCLATE: GB358
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 129:

Val Tyr Glu Thr Glu His His Ile Leu His Leu 1 5 10

(2) INFORMATION FOR SEQ ID NO: 130:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 11 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (vi) ORIGINAL SOURCE:
  - (A) CRGANISM: amino acid
  - (C) INDIVIDUAL ISOLATE: GB549
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 130:

Val Tyr Glu Ala Asp His His Ile Met His Leu 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 131:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 11 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (iii) HYPOTHETICAL: NO
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: amino acid
    - (C) INDIVIDUAL ISCLATE: GB809
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 131:

Val Tyr Glu Thr Asp His His Ile Leu His Leu 1  $\phantom{\bigg|}$  5

- (2) INFORMATION FOR SEQ ID NO: 132:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 13 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (iii) HYPOTHETICAL: NO
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: amino acid
    - (C) INDIVIDUAL ISOLATE: GB358

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 132:
- Val Arg Val Gly Asn Gln Ser Arg Cys Trp Val Ala Leu 1 5 10
- (2) INFORMATION FCR SEQ ID NO: 133:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 13 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (iii) HYPOTHETICAL: NO
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: amino acid
    - (C) INDIVIDUAL ISOLATE: GB549
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 133:

Val Arg Thr Gly Asm Thr Ser Arg Cys Trp Val Pro Leu

1 5 10

- (2) INFORMATION FOR SEQ ID NO: 134:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 13 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (iii) HYPOTHETICAL: NO
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: amino acid
    - (C) INDIVIDUAL ISOLATE: GB809
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 134:

Val Arg Ala Gly Asm Val Ser Arg Cys Trp Thr Pro Val 1

- (2) INFORMATION FOR SEQ ID NO: 135:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino ācids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: amino acid
  - (C) INDIVIDUAL ISOLATE: GB358
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 135:

Ala Pro Tyr Ile Gly Ala Pro Leu Glu Ser
1 5 10

- (2) INFORMATION FOR SEQ ID NO: 136:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (iii) HYPOTHETICAL: NO
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: amino acid
    - (C) INDIVIDUAL ISOLATE: GB549
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 136:

Ala Pro Tyr Val Gly Ala Pro Leu Glu Ser 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 137:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (iii) HYPOTHETICAL: NO
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: amino acid
    - (C) INDIVIDUAL ISOLATE: GB809
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 137:

Ala Val Ser Met Asp Ala Pro Leu Glu Ser
1 5 10

(2) INFORMATION FOR SEQ ID NO: 138:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 10 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (11) MOLECULE TUPE: peptide
- (iii) HYPOTHETICAL: NO
- (V1) ORIGINAL SOURCE:
  - (A) ORGANISM: amino acid
  - (C) INDIVIDUAL ISCLATE: GB358 and GB809
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 138:

Gln Pro Arg Arg His Trp Thr Thr Gln Asp 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 139:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (iii) HYPOTHETICAL: NO
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: amino acid
    - (C) INDIVIDUAL ISOLATE: GB549
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 139:

Arg Pro Arg Arg His Trp Thr Thr Gln Asp 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 140:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (111) HYPOTHETICAL: NO
  - (vi) ORIGINAL SOURCE:

- (A) ORGANISM: amino acid(C) INDIVIDUAL ISOLATE: GB549
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 140:

Arg Pro Arg Arg His Trp Thr Thr Gln Asp 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 141:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 23 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA
  - (iii) HYPOTHETICAL: NO
  - (ill) ANTI-SENSE: NO
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 141:

TGGGATATGA TGATGAACTG GTC

23

- (2) INFORMATION FOR SEQ ID NO: 142:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 24 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
    - (ii) MOLECULE TYPE: cDNA
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: YES
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 142:

CCAGGTACAA CCGAACCAAT TGCC

24

- (2) INFORMATION FOR SEQ ID NO: 143:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 957 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear

(ii)	MOLECULE	TYPE:	CDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

#### (ix) FEATURE:

(A) NAME/KEY: CDS
(B) LOCATION: 1..957

#### (ix) FEATURE:

(A) NAME/KEY: mat_peptide
(B) LOCATION: 1..954

## (X1) SEQUENCE DESCRIPTION: SEQ ID NO: 143:

-															
					AAA Lys										43
-					GTC Val										96
					CCG Pro										144
					GAG Glu										192
					CGC Arg 70										240
					TAC Tyr										288
				Arg	GGG Gly				Ser						336
			Ser					Lys					Leu	TGT Cys	384
		Ala					Tyr					. Gly		GTT Val	432
	Gly					Leu					. Arg			A GAC 1 Asp 160	480

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	TAT TYT									<b>5</b> 28
	GCC Ala 180									576
	AAC Asn									624
	ATC Ile									672
	CCT								-	720
	Pro									768
	ACG Thr 260									816
	TAC Tyr									864
			Gln			Val		TGC Cys		912
Cys	 ATA Ile				His					957

- (2) INFORMATION FOR SEQ ID NO: 144:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 319 amino acids
    - (B) TYPE: amino acid
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 144:

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn 1  $\phantom{\bigg|}$  5  $\phantom{\bigg|}$  10  $\phantom{\bigg|}$  15

Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gln Ile Val Gly 20 25 30

- Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala 35 40 45
- Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro 50 55 60
- Ile Pro Lys Asp Arg Arg Pro Thr Gly Lys Ser Trp Gly Lys Pro Gly
  65 75 80
- Tyr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Leu Gly Trp Ala Gly Trp 85 90 95
- Leu Leu Ser Pro Arg Gly Ser Arg Pro Ser Trp Gly Pro Thr Asp Pro
- Arg His Arg Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys
  115 120 125
- Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Val Val Gly Ala Pro Val 130 135 140
- Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu Glu Asp 145 150 155 160
- Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe Ser Ile 165 170 175
- Phe Leu Leu Ala Leu Leu Ser Cys Ile Thr Val Pro Val Ser Gly Leu 180 185 190
- Gln Val Lys Asn Thr Ser Ser Ser Tyr Met Val Thr Asn Asp Cys Gln
  195 200 205
- Asn Ser Ser Ile Val Trp Gln Leu Arg Asp Ala Val Leu His Val Pro 210 215 220
- Gly Cys Val Pro Cys Glu Glu Lys Gly Asn Ile Ser Arg Cys Trp Ile 225 230 235 240
- Pro Val Ser Pro Asn Ile Ala Val Ser Gln Pro Gly Ala Leu Thr Lys 245 250 255
- Gly Leu Arg Thr His Ile Asp Thr Ile Ile Ala Ser Ala Thr Phe Cys 260 265 270
- Ser Ala Leu Tyr Ile Gly Asp Leu Cys Gly Ala Val Met Leu Ala Ser 275 280 285
- Gln Val Phe Ile Ile Ser Pro Gln His His Lys Phe Val Gln Asp Cys 290 295 300
- Asn Cys Ser Ile Tyr Pro Gly His Ile Thr Gly His Arg Met Ala 305 310 315
- (2) INFORMATION FOR SEQ ID NO: 145:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 340 base pairs

<ul><li>(B) TYPE: nucleic acid</li><li>(C) STRANDEDNESS: single</li><li>(D) TOPOLOGY: linear</li></ul>	
(ii) MOLECULE TYPE: CDNA	
(iii) HYPOTHETICAL: NO	
(iii) ANTI-SENSE: NO	
(ix) FEATURE:  (A) NAME/KEY: mat_peptide  (B) LOCATION: 2337	
(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 2340	
(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 145:	
C TCA ACG GTC ACG GAG AGG GAC ATC AGA ACT GAG GAG TCC ATA TAC Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Ser Ile Tyr 1 5 10 15	46
CTT GCT TGC TCT TTA CCC GAG CAG GCA CGG ACT GCC ATA CAC TCA CTG Leu Ala Cys Ser Leu Pro Glu Gln Ala Arg Thr Ala Ile His Ser Leu 20 25 30	94
ACT GAG AGG CTT TAC GTG GGA GGG CCC ATG CTA AAC AGC AAA GGG CAA Thr Glu Arg Leu Tyr Val Gly Gly Pro Met Leu Asn Ser Lys Gly Gln 35 40 45	142
ACC TGC GGA TAC AGA CGC TGC CGC GCC AGC GGA GTG TTC ACC ACT AGC Thr Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser 50 55 60	190
ATG GGA AAT ACC ATC ACG TGC TAC GTG AAG GCA CAA GCA GCC TGT AAG Met Gly Asn Thr Ile Thr Cys Tyr Val Lys Ala Gln Ala Ala Cys Lys 65 70 75	238
GCT GCG GGC ATA ATT GCC CCC ACG ATG CTG GTG TGC GGC GAC GAT CTA Ala Ala Gly Ile Ile Ala Pro Thr Met Leu Val Cys Gly Asp Asp Leu 80 85 90 95	286
GTT GTC ATC TCA GAG AGT CAG GGG ACC GAG GAG GAC GAG CGG AAC CTA Val Val Ile Ser Glu Ser Gln Gly Thr Glu Glu Asp Glu Arg Asn Leu 100 105 110	334
CGA GCC	340

#### (2) INFORMATION FOR SEQ ID NO: 146:

Arg Ala

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 146:

Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Ser Ile Tyr Leu 1 5 10 15

Ala Cys Ser Leu Pro Glu Gln Ala Arg Thr Ala Ile His Ser Leu Thr 20 25 30

Glu Arg Leu Tyr Val Gly Gly Pro Met Leu Asn Ser Lys Gly Gln Thr 35 40 45

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser Met 50 55 60

Gly Asn Thr Ile Thr Cys Tyr Val Lys Ala Gln Ala Ala Cys Lys Ala 65 70 75 80

Ala Gly Ile Ile Ala Pro Thr Met Leu Val Cys Gly Asp Asp Leu Val

Val Ile Ser Glu Ser Gln Gly Thr Glu Glu Asp Glu Arg Asm Leu Arg 100 105 110

Ala

- (2) INFORMATION FOR SEQ ID NO: 147:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 345 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: NO
  - (ix) FEATURE:
    - (A) NAME/KEY: CDS
    - (B) LOCATION: 1..345
  - (ix) FEATURE:
    - (A) NAME/KEY: mat_peptide
    - (B) LOCATION: 1..342
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 147:

ATG AGC ACA CTT CCT AAA CCA CAA AGA AAA ACC AAA AGA AAC ACC AAC

Met 1	Ser	Thr	Leu	Pro 5	Lys	Pro	Gln	Arg	Lys 10	Thr	Lys	Arg	Asn	Thr 15	Asn	
					TTA Leu											96
					CAC His											144
					AGC Ser							-				192
					GAA Glu 70											240
					ATG Met											288
					GCT											336
		GGA Gly 115														345

## (2) INFORMATION FOR SEQ ID NO: 148:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 115 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 148:

Met Ser Thr Leu Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn 1 5 10 15

Pro Gly His Arg Thr Leu Ser Ser Gln Ala Ala Val Arg Ser Leu Val 20 25 30

Glu Phe Thr Cys Tyr His Ala Gly Ala Pro Ser Trp Val Cys Val Gln 35 40 45

Cys Ala Arg Leu Pro Ser Gly Arg Asn Leu Ala Val Gly Ala Asn Pro 50 60

Ser Pro Gly Arg Ala Glu Pro Arg Ala Gly Pro Gly Leu Ser Pro Gly 65 70 75 80

Thr Leu Gly Pro Tyr Met Gly Met Arg Ala Ala Gly Gly Gln Gly Gly

90

Ser Cys Pro Arg Ala Ala Leu Ala Arg Arg Gly Ala Gln Met Thr Pro

100 105 110

Gly Ala Gly

(2) INFORMATION FOR SEQ ID NO: 149:

85

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 280 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
  - (A) NAME/KEY: CDS
  - (B) LOCATION: 2..280
- (ix) FEATURE:
  - (A) NAME/KEY: mat_peptide
  - (B) LOCATION: 2..277
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 149:
- G GCC TGT GAC CTC AAG GAC GAG GCT AGG AGG GTG ATA ACT TCA CTC

  Ala Cys Asp Leu Lys Asp Glu Ala Arg Arg Val Ile Thr Ser Leu

  1 5 10 15
- ACG GAG CGG CTT TAC TGT GGT GGT CCT ATG TTC AAC AGC AAG GGA CAA 94
  Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly Gln
  20 25 30
- CAC TGC GGT TAC CGC CGC TGC CGT GCT AGT GGG GTG CTA CCC ACC AGC

  His Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr Ser

  35

  40

  45
- TTC GGG AAC ACA ATC ACC TGT TAC ATC AAA GCA AAG GCA GCT ACC AAA

  190
  Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Lys Ala Ala Thr Lys
  50
  55
  60
- GCT GCC GGA ATT AAA AAT CCA TCA TTC CTT GTC TGC GGA GAT GAC TTG

  Ala Ala Gly Ile Lys Asn Pro Ser Phe Leu Val Cys Gly Asp Asp Leu

  70

  75
- GTC GTG ATT GCT GAG AGT GCA GGG ATC GAT GAG GAC AGA GCG
  Val Val Ile Ala Glu Ser Ala Gly Ile Asp Glu Asp Arg Ala
  80 85 90
- (2) INFORMATION FOR SEQ ID NO: 150:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 93 amino acids

- (B) TYPE: amino acid
  (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 150:

Ala Cys Asp Leu Lys Asp Glu Ala Arg Arg Val Ile Thr Ser Leu Thr
1 10 15

Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly Gln His 20 25 30

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr Ser Phe

Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Lys Ala Ala Thr Lys Ala 50 55 60

Ala Gly Ile Lys Asn Pro Ser Phe Leu Val Cys Gly Asp Asp Leu Val 65 70 75 80

Val Ile Ala Glu Ser Ala Gly Ile Asp Glu Asp Arg Ala 85 90

- (2) INFORMATION FOR SEQ ID NO: 151:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 499 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: NO
  - (ix) FEATURE:
    - (A) NAME/KEY: CDS
    - (B) LOCATION: 1..499
  - (ix) FEATURE:
    - (A) NAME/KEY: mat_peptide
    - (B) LOCATION: 1..496
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 151:

ATG AGC ACG AAT CCT AAA CCT CAA AGA AAA ACC AAA AGA AAC ACC AAC

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn

1 5 10 15

CGT CGC CCA CAG GAC GTC AAG TTC CCG GGC GGT GGT CAG ATC GTT GGC

Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly

20

25

30

		CCG Pro								144
		GAA Glu								192
		CAG Gln 70								240
		TAC Tyr								288
		GGC Gly							-	336
		AAT Asn								384
		ATG Met								432
		GCT Ala 150						GAC Asp 160		480
-	 TAT Tyr	 ACA Thr	G							499

#### (2) INFORMATION FOR SEQ ID NO: 152:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 166 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 152:

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn

Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gln Ile Val Gly
20 25 30

Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Met Gly Val Arg Ala

	•	202									
Thr Arg Lys 50	Thr Ser Glu Arg S	=	ly Arg Arg Gln 60	Pro							
Ile Pro Lys 65	Ala Arg Gln Pro T 70	Thr Gly Arg Ser T 75	rp Gly Gln Pro	Gly 80							
Tyr Pro Trp	Pro Leu Tyr Ala A 85	Asn Glu Gly Leu G 90	ly Trp Ala Gly 95	Trp							
Leu Leu Ser	Pro Arg Gly Ser 2	Arg Pro Asn Trp G 105	ly Pro Asn Asp	Pro							
Arg Arg Lys 115	Ser Arg Asn Leu C	Gly Lys Val Ile A 120	sp Thr Leu Thr 125	Cys							
Gly Phe Ala 130	Asp Leu Met Gly 3	- <del>-</del>	Tal Gly Gly Pro	Ile							
	Ala Arg Ala Leu i			Asp . 160							
Gly Val Asn	Tyr Ala Thr 165										
(2) INFORMA	TION FOR SEQ ID NO	C: 153:									
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 579 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear											
(ii) MO	LECULE TYPE: cDNA										
(iii) HY	POTHETICAL: NO										
(iii) AN	TI-SENSE: NO										
	ATURE: A) NAME/KEY: CDS B) LOCATION: 15	579									
	ATURE:  A) NAME/KEY: mat_ B) LOCATION: 15										
(xi) SE	QUENCE DESCRIPTION	ON: SEQ ID NO: 15	3:	•							
	TTC GCC GAT CTC Phe Ala Asp Leu 5	· ·	=	g Gly							
	G GGC GTC GCA AGG V Gly Val Ala Arg 20										

GAG GAC GGG GTA AAC TAT, CCA ACA GGG AAT TTA CCC GGT TGC TCT TTC 144

Glu	Asp	Gly 35	Val	Asn	Tyr	Pro	Thr 40	Gly	Asn	Leu	Pro	Gly 45	Cys	Ser	Phe		
TOT	a TC	بلملمذ	מדיד	لمشت	CCT	ىسىت	CTC	TCG	тст	CTG	אכיר	حست	CCG	GCC	тст		192
								Ser									
301	50	2110	1.0			55	-		<b>-</b> 70		60						
GCA	GTT	CCC	TAC	CGA	AAT	GCC	TCT	GGG	ATT	TAT	CAT	GTT	ACC	AAT	GAT		240
Ala	Val	Pro	Tyr	Arg	Asn	Ala	Ser	Gly	Ile	Tyr	His	Val	Thr	Asn	qzA		
<del>6</del> 5					70					75					80		
TGC	CCA	AAC	TCT	TCC	ATA	GTC	TAT	GAG	GCA	GAT	AAC	CTG	DTA	CTA	CAC		238
Cys	Pro	Asn	Ser	Ser	Ile	Val	Tyr	Glu	Ala	Asp	Asn	Leu	Ile	Leu	His		
				85					90					95			
GCA	CCT	GGT	TGC	GTG	CCT	TGT	GTC	ATG	ACA	GGT	AAT	GTG	AGT	AGA	TGC		336
Ala	Pro	Gly	Cys	Val	Pro	Cys	Val	Met	Thr	Gly	Asn	Val	Ser	Arg	Cys		
			100					105					110			-	
TGG	GTC	CAA	ATT	ACC	CCT	ACA	CTG	TCA	GCC	CCG	AGC	CTC	GGA	GCA	GTC		384
Trp	Val	Gln	Ile	Thr	Pro	Thr	Leu	Ser	Ala	Pro	Ser	Leu	Gly	Ala	Val		
		115					120					125					
ACG	GCT	CCT	CTT	CGG	AGA	GCC	GTT	GAC	TAC	CTA	GCG	GGA	GGG	GCT	GCC		432
Thr	Ala	Pro	Leu	Arg	Arg	Ala	Val	Asp	Tyr	Leu	Ala	Gly	Gly	Ala	Ala		
	130					135					140						
CTC	TGC	TCC	GCG	TTA	TAC	GTA	GGA	GAC	GCG	TGT	GGG	GCA	CTA	TTC	TTG		480
Leu	Cys	Ser	Ala	Leu	Tyr	Val	Gly	Asp	Ala	Cys	Gly	Ala	Leu	Phe	Leu		
145					150					155					160		
GTA	GGC	CAA	ATG	TTC	ACC	TAT	AGG	CCT	CGC	CAG	CAC	GCT	ACG	GTG	CAG		523
Val	Gly	Gln	Met	Phe	Thr	Tyr	Arg	Pro	Arg	Gln	Hls	Ala	Thr	Val	Gln		
				165					170					175			
AAC	TGC	AAC	TGT	TCC	ATT	TAC	AGT	GGC	CAT	GTT	ACC	GGC	CAC	CGG	ATG		576
Asn	Cys	Asn	Cys	Ser	Ile	Тут	Ser	Gly	His	Val	Thr	Gly	Hls	Arg	Met		
			180					185					190				
GCG																	579
Ala																	

#### (2) INFORMATION FOR SEQ ID NO: 154:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 193 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 154:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly
1 5 10 15

- Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu 20 25 30
- Glu Asp Gly Val Asn Tyr Pro Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45
- Ser Ile Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55
- Ala Val Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp 65 70 75 80
- Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asn Leu Ile Leu His 85 90 95
- Ala Pro Gly Cys Val Pro Cys Val Met Thr Gly Asn Val Ser Arg Cys
- Trp Val Gln Ile Thr Pro Thr Leu Ser Ala Pro Ser Leu Gly Ala Val 115 120 125
- Thr Ala Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala Gly Gly Ala Ala 130 135 140
- Leu Cys Ser Ala Leu Tyr Val Gly Asp Ala Cys Gly Ala Leu Phe Leu 145 150 155 160
- Val Gly Gln Met Phe Thr Tyr Arg Pro Arg Gln His Ala Thr Val Gln 165 170 175
- Asn Cys Asn Cys Ser Ile Tyr Ser Gly His Val Thr Gly His Arg Met 180 185 190

Ala

- (2) INFORMATION FOR SEQ ID NO: 155:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 579 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (i1) MOLECULE TYPE: cDNA
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: NO
    - (ix) FEATURE:
      - (A) NAME/KEY: CDS
      - (B) LOCATION: 1..579
    - (1x) FEATURE:
      - (A) NAME/KEY: mat_peptide
      - (B) LOCATION: 1..575

(xi) SEQUENC	E DESCRIPTION:	SEQ	ID	NO:	155:	
--------------	----------------	-----	----	-----	------	--

							GGG		_					48
							CTC Leu 25							96
							GGG Gly							144
							TCG Ser				_	_		192
							GGG Gly							240
							GAG Glu							288
							AGG Arg 105							336
							TCA Ser							384
						Val					Gly		GCC Ala	432
	Cys				Val					Gly			TTG Leu 160	480
				Thr					Gln				CAG Gln	528
			Sex					/ His				Glr	ATG 1 Met	576
GCA Ala														579

⁽²⁾ INFORMATION FOR SEQ ID NO: 156:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 193 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 156:

Thr Cys Gly Phe Ala Asp Leu Val Gly Tyr Ile Pro Leu Val Gly Gly
1 5 10 15

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu
20 25 30

Glu Asp Gly Val Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

Ser Ile Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55 60

Ala Val Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Leu Ile Leu His 85 90 95

Ala Pro Gly Cys Val Pro Cys Val Arg Lys Asp Asn Val Ser Arg Cys
100 105 110

Trp Val Gln Ile Thr Pro Thr Leu Ser Ala Pro Ser Phe Gly Ala Val

Thr Ala Pro Leu Arg Arg Ala Val Asp Tyr Leu Val Gly Gly Ala Ala 130 140

Leu Cys Ser Ala Leu Tyr Val Gly Asp Ala Cys Gly Ala Leu Phe Leu 145 150 155 160

Val Gly Gln Met Phe Thr Tyr Arg Pro Arg Gln His Ala Thr Val Gln 165 170 175

Asp Cys Asn Cys Ser Ile Tyr Ser Gly His Val Thr Gly His Gln Met 180 185 190

Ala

- (2) INFORMATION FOR SEQ ID NO: 157:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 530 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA

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(iii) HYPOTHETICAL: NO												
(iii) ANTI-SENSE: NO												
(ix) FEATURE:  (A) NAME/KEY: CDS  (B) LOCATION: 3530  (ix) FEATURE:  (A) NAME/KEY: mat_peptide  (B) LOCATION: 3527												
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 157:												
CA CCT ACG ACA GCT CTG CTG GTG GCC CAG TTA CTG CGG ATT CCC CAA  Pro Thr Thr Ala Leu Leu Val Ala Gln Leu Leu Arg Ile Pro Gln  1 5 13 15	47											
GTG GTC ATT GAC ATC ATC GCA GGG AGC CAC TGG GGG GTC TTG TTT GCC Val Val Ile Asp Ile Ile Ala Gly Ser His Trp Gly Val Leu Phe Ala 20 25 30	95											
GCC GCA TAC TAT GCA TCG GTG GCT AAC TGG ACC AAG GTC GTG CTG GTC Ala Ala Tyr Tyr Ala Ser Val Ala Asn Trp Thr Lys Val Val Leu Val 35 40 45	143											
TTG TTT CTG TTT GCA GGG GTT GAT GCT ACT ACC CAG ATT TCG GGC GGC Leu Phe Leu Phe Ala Gly Val Asp Ala Thr Thr Gln Ile Ser Gly Gly 50 55 60	191											
TCC AGC GCC CAA ACG ACG TAT GGC ATC GCC TCA TTT ATC ACC CGC GGC Ser Ser Ala Gln Thr Thr Tyr Gly Ile Ala Ser Phe Ile Thr Arg Gly 65 70 75	239											
GCG CAG CAG AAA CTG CAG CTC ATA AAT ACC AAC GGA AGC TGG CAC ATC Ala Gln Gln Lys Leu Gln Leu Ile Asn Thr Asn Gly Ser Trp His Ile 80 85 90 95	287											
AAC AGG ACC GCC CTT AAT TGT AAT GAC AGC CTC CAG ACT GGG TTC ATA Asn Arg Thr Ala Leu Asn Cys Asn Asp Ser Leu Gln Thr Gly Phe Ile 100 105 110	335											
GCC GGC CTC TTC TAC TAC CAT AAG TTC AAC TCT TCT GGA TGC CCG GAT Ala Gly Leu Phe Tyr Tyr His Lys Phe Asn Ser Ser Gly Cys Pro Asp 115 120 125	383											
CGG ATG GCT AGC TGT AGG GCC CTT GCC ACT TTT GAC CAG GGC TGG GGA Arg Met Ala Ser Cys Arg Ala Leu Ala Thr Phe Asp Gln Gly Trp Gly 130 135 140	431											
ACT ATC AGC TAT GCC AAC ATA TCG-GGT CCC AGT GAT GAC AAA CCA TAT Thr Ile Ser Tyr Ala Asn Ile Ser Gly Pro Ser Asp Asp Lys Pro Tyr 145 150 155	479											
TGC TGG CAC TAT CCC CCA CGG CCG TGC GGA GTG GTG CCA GCC CAA GAG	527											

Cys Trp His Tyr Pro Pro Arg Pro Cys Gly Val Val Pro Ala Gln Glu 160 165 170 175

GTC Val

530

- (2) INFORMATION FOR SEQ ID NO: 158:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 176 amino acids
    - (B) TYPE: amine acid
    - (D) TOPOLOGY: .linear
  - (ii) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 158:

Pro Thr Thr Ala Leu Leu Val Ala Gln Leu Leu Arg Ile Pro Gln Val 1 5 15

Val Ile Asp Ile Ile Ala Gly Ser His Trp Gly Val Leu Phe Ala Ala 20 25 30

Ala Tyr Tyr Ala Ser Val Ala Asn Trp Thr Lys Val Val Leu Val Leu 35 40 45

Phe Leu Phe Ala Gly Val Asp Ala Thr Thr Gln Ile Ser Gly Gly Ser 50 60

Ser Ala Gln Thr Thr Tyr Gly Ile Ala Ser Phe Ile Thr Arg Gly Ala 65 70 75 80

Gln Gln Lys Leu Gln Leu Ile Asn Thr Asn Gly Ser Trp His Ile Asn 90

Arg Thr Ala Leu Asn Cys Asn Asp Ser Leu Gln Thr Gly Phe Ile Ala 100 105 110

Gly Leu Phe Tyr Tyr His Lys Phe Asn Ser Ser Gly Cys Pro Asp Arg 115 120 125

Met Ala Ser Cys Arg Ala Leu Ala Thr Phe Asp Gln Gly Trp Gly Thr 130 135 140

Trp His Tyr Pro Pro Arg Pro Cys Gly Val Val Pro Ala Gln Glu Val 165 170 175

- (2) INFORMATION FOR SEQ ID NO: 159:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 340 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single

(D) TOPOLOGY: linear
----------------------

(i1) MOLECULE TYPE: cDNA

(111) HYPCTHETICAL: NO

(iii) ANTI-SENSE: NO

# (ix) FEATURE:

(A) NAME/KEY: CDS
(B) LOCATION: 2..340

#### (1x) FEATURE:

(A) NAME/KEY: mat_peptide (B) LOCATION: 2..337

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 159:

	G ACC G Thr V				t Th			e Ty	46	õ
	ICA TGT Ser Cys								. 94	*
	CAA CGC Gln Arg						 		 142	2
	IGT GGT Cys Gly 50	Tyr							190	כ
	GGC AAC Gly Asn 65								238	3
	GCA AGG Ala Arg						 		 28	6
	GCC ATO Ala Ile								33	4
AGA (									34	0

## (2) INFORMATION FOR SEQ ID NO. I60:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 113 amino acids
  - (B) TYPE: amino acid

- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 160:

Ser Thr Val Thr Glu His Asp Ile Met Thr Glu Glu Ser Ile Tyr Gln 1 5 10 15

Ser Cys Asp Leu Gln Pro Glu Ala Arg Ala Ala Ile Arg Ser Leu Thr 20 25 30

Gln Arg Leu Tyr Cys Gly Gly Pro Met Tyr Asn Ser Lys Gly Gln Gln 35 40 45

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser Met
50 55 60

Gly Asn Thr Met Thr Cys Tyr Ile Lys Ala Leu Ala Ser Cys Arg Ala 65 70 75 80

Ala Arg Leu Arg Asp Cys Thr Leu Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Ala Ile Cys Glu Ser Gln Gly Thr His Glu Asp Glu Ala Ser Leu Arg
100 105 110

Ala

- (2) INFORMATION FOR SEQ ID NO: 161:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 340 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: NO
  - (ix) FEATURE:
    - (A) NAME/KEY: CDS
    - (B) LOCATION: 2..340
  - (ix) FEATURE:
    - (A) NAME/KEY: mat_peptide
    - (B) LOCATION: 2..337
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 161:
- C TCA ACC GCC ACC GAA CAT GAC ATA TTG ACT GAA GAG TCC ATA TAC Ser Thr Ala Thr Glu His Asp Ile Leu Thr Glu Glu Ser Ile Tyr

	1				5				:	10				:	15		
CAA Gln	TCA Ser	<b>T</b> GT Cys	GAC Asp	TCG Ser 20	CAG Gln	CCC	GAC Asp	GCA Ala	CGC Arg 25	GCA Ala	GCA Ala	ATA Ile	CGG Arg	TCA Ser 30	CTC Leu		94
ACC	CAA Gln	CGC Arg	TTG Leu 35	TTC Phe	TGT Cys	GGA Gly	GGC Gly	CCC Pro 40	ATG Met	TAT Tyr	AAC Asn	AGC Ser	AAG Lys 45	GGG Gly	CAA Glm		142
CAA Gln	TGT Cys	GGT Gly 50	TAT Tyr	CGC Arg	AGA Arg	TGC Cys	CGC Arg 55	GCC Ala	AGC Ser	GGC Gly	GTC Val	TTC Phe 60	ACC Thr	ACC Thr	AGT Ser		190
ATG Met	GGC Gly 65	<b>A</b> AC <b>A</b> sn	ACC Thr	ATG Met	ACG Thr	TGC Cys 70	TAC Tyr	ATT Ile	AAG Lys	GCT Ala	TTA Leu 75	GCC Ala	TCC Ser	TGT Cys	AGA Arg		238
ACC Thr 80	GCT Ala	<b>G</b> GG <b>G</b> ly	CTC Leu	CGG Arg	GAC Asp 85	TAC Tyr	ACG Thr	CTC Leu	CTG Leu	GTG Val 90	TGT Cys	GGT Gly	GAC Asp	GAT Asp	CAT His 95	•	286
GTG Val	GCC Ala	ATC Ile	TGC Cys	GAG Glu 100	AGC Ser	CAG Gln	GGG Gly	ACA Thr	CAC His 105	GAG Glu	GAT Asp	GAA Glu	GCG Ala	AAC Asn 110	CTG Leu		334
AGA Arg																	340

#### (2) INFORMATION FOR SEQ ID NO: 162:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 113 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 162:

Ser Thr Ala Thr Glu His Asp Ile Leu Thr Glu Glu Ser Ile Tyr Gln 1 5 10 15

Ser Cys Asp Ser Gln Pro Asp Ala Arg Ala Ala Ile Arg Ser Leu Thr 20 25 30 Gln Arg Leu Phe Cys Gly Gly Pro Met Tyr Asn Ser Lys Gly Gln Gln

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser Met

Gly Asn Thr Met Thr Cys Tyr Ile-Lys Ala Leu Ala Ser Cys Arg Thr
65 70 75 80

Ala Gly Leu Arg Asp Tyr Thr Leu Leu Val Cys Gly Asp Asp His Val

Ala Ile Cys Glu Ser Gln Gly Thr His Glu Asp Glu Ala Asn Leu Arg 100 105 110

Ala

- (2) INFORMATION FOR SEQ ID NO: 163:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 499 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: NO
  - (1x) FEATURE:
    - (A) NAME/KEY: CDS
    - (B) LOCATION: 1..499
  - (ix) FEATURE:
    - (A) NAME/KEY: mat_peptide
    - (B) LOCATION: 1..496
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 163:

AT	'G A	\GC	ACG	AAT	CCT	AAA	CII	CAA	AGA	AAA	ACC	AAA	CGT	AAC	ACC	AAC	48	
M∈	t S	er	Thr	Asn	Pro	Lys	Leu	Gln	Arg	Lys	Thr	Lys	Arg	Asn	Thr	Asn		
	1				_				•	10		•	_		15			

- CGC CGC CCC ATG GAC GTT AAG TTC CCG GGT GGT GGC CAG ATC GTT GGC
  Arg Arg Pro Met Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly
- GGA GTT TAC TTG TTG CCG CGC AGG GGC CCT AGG TTG GGT GTG CGC GCG GGG GI GI GI Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala
- ACT CGG AAG ACT TCG GAG CGG TCG CAA CCT CGT GGG AGG CGC CAA CCT 192
  Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro
  50 55 60
- ATC CCC AAG GCG CGC CGA TCC GAG GGC AGA TCC TGG GCG CAG CCC GGG

  Ile Pro Lys Ala Arg Arg Ser Glu Gly Arg Ser Trp Ala Gln Pro Gly
  65 70 75 80
- TAT CCT TGG CCC CTT TAC GGC AAT GAG GGC TGT GGG TGG GCA GGG TGG

  Tyr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp

  85

  90

  95
- CTC CTG TCC CCT CGC GGG TCT CGG CCG TCT TGG GGC CCT AAT GAT CCC 336

Leu	Leu	Ser	Pro 100	Arg	Gly	Ser	Arg	Pro 105	Ser	Trp	Gly	Pro	Asn 110	qzA	Pro		
					AAC Asn												384
					ATG Met												432
					GCC Ala 150												480
				GCA Ala 165	ACA Thr	G										-	499

- (2) INFORMATION FOR SEQ ID NO: 164:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 166 amino acids
    - (B) TYPE: amino acid
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 164:

Met Ser Thr Asn Pro Lys Leu Gln Arg Lys Thr Lys Arg Asn Thr Asn 1 10 15

Arg Arg Pro Met Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly

Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala

Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro 50 55 60

Ile Pro Lys Ala Arg Arg Ser Glu Gly Arg Ser Trp Ala Gln Pro Gly 65 70 75 80

Tyr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp 85 90 95

Leu Leu Ser Pro Arg Gly Ser Arg Pro Ser Trp Gly Pro Asn Asp Pro 100 105 110

Arg Arg Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys
115 120 - 125

Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala Pro Val 130 135 140

Gly	Gly	Val	Ala	Arg	Ala	Leu	Ala	His	Gly	Val	Arg	Ala	Val	Glu	Asp
145					150					155					160

Gly Ile Asn Tyr Ala Thr 165

- (2) INFORMATION FOR SEQ ID NO: 165:
  - (1) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 499 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: DNA (genomic)
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: NO
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 165:

ATGAGCACGA	ATCCTAAACC	TCAAAGAAAA	ACCAAACGTA	ACACCAACCG	CCGCCCTATG	60
GACGTTAAGT	TCCCAGGCGG	TGGTCAGATC	GTTGGCGGAG	TTTACTTGTT	GCCGCGCAGG	120
GGCCCCAGGT	TGGGTGTGCG	CGCGACTCGG	AAGACTTCGG	AGCGGTCGCA	ACCTCGTGGG .	180
AGGCGCCAAC	CTATCCCCAA	GGCGCGCCGA	ACCGAGGGCA	GATCCTGGGC	GCAGCCCGGG	240
TATCCTTGGC	CCCTTTACGG	CAATGAGGGC	TGTGGGTGGG	CAGGGTGGCT	CCTGTCCCCT	300
CGCGGNTCTC	GGNCGTCTTG	GGGCCCCAAT	GATCCCCGGN	GGAGATCCCG	CAACTTGGGT	360
AAGGTCATCG	ATACCCTAAC	ATGCGGCTTC	GCCGACCTCA	TGGGATACAT	CCCGCTTGTA	420
GGCGCCCCG	TGGGTGGCGT	CGCCAGGGCC	CTGGCACATG	GTGTTAGGGC	TGTGGAAGAC	480
GGGATCAATT	ATGCAACAG					499

- (2) INFORMATION FOR SEQ ID NO: 166:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 126 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 166:

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn

215 Arg Arg Pro Met Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly 25 Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro Ile Pro Lys Ala Arg Arg Thr Glu Gly Arg Ser Trp Ala Gln Pro Gly Tyr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp 90 Leu Leu Ser Pro Arg Xaa Ser Arg Xaa Ser Trp Gly Pro Asn Asp Pro 105 Arg Xaa Arg Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu 120 (2) INFORMATION FOR SEQ ID NO: 167: (1) SEQUENCE CHARACTERISTICS: (A) LENGTH: 579 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: cDNA (iii) HYPOTHETICAL: NO (iii) ANTI-SENSE: NO (ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 1..579 (ix) FEATURE: (A) NAME/KEY: mat_peptide (B) LOCATION: 1..579 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 167: ACA TGC GGC TTC GCC GAC CTC ATG GGA TAC ATC CCG CTT GTA GGC GCC 48 Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala CCC GTG GGT GGC GTC GCC AGG GCC-CTG GCA CAT GGT GTT AGG GCT GTG 96 Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val

25

GAA GAC GGG ATC AAT TAT GCA ACA GGG AAC CTT CCC GGT TGC TCC TTT

Glu	Asp	Gly 35	Ile	Asn	Tyr	Ala	Thr 40	Gly	Asn	Leu	Pro	Gly 45	Cys	Ser	Phe		
TCT Ser	ATC Ile 50	TTC Phe	CTC Leu	TTG Leu	GCG Ala	CTC Leu 55	CTC	TCG Ser	TGC Cys	CTG Leu	ACT Thr 60	GTT Val	CCC Pro	ACA Thr	TCG Ser		192
GCC Ala 65	GTT Val	AAC Asn	TAT Tyr	CGC <b>Ar</b> g	AAT Asn 70	GCT Ala	TCG Ser	GGC Gly	ATT Ile	TAT Tyr 75	CAC His	ATC Ile	ACC Thr	AAT Asn	GAC QaA 08		240
TGC Cys	CCG Pro	AAT Asn	GCA Ala	AGC Ser 85	ATA Ile	GTG Val	TAC Tyr	GAG Glu	ACC Thr 90	GAA Glu	AAT Asn	CAC His	ATC Ile	TTA Leu 95	CAC H1s		288
						TGT Cys										-	336
						ACA Thr											384
						CAT His 135											432
						ATC Ile											480
						TTC Phe											528
						TAC Tyr											576
GCA																	579

### (2) INFORMATION FOR SEQ ID NO: 163:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 193 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (11) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 168:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala 1 5 10 15 Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Thr Ser 50 55 60

Ala Val Asn Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile Thr Asn Asp 65 70 75 80

Cys Pro Asn Ala Ser Ile Val Tyr Glu Thr Glu Asn His Ile Leu His
85 90 95

Leu Pro Gly Cys Val Pro Cys Val Arg Thr Gly Asn Gln Ser Arg Cys
100 105 110

Trp Val Ala Leu Thr Pro Thr Val Ala Ser Pro Tyr Ala Gly Ala Pro 115 120 125

Leu Glu Pro Leu Arg Arg His Val Asp Leu Met Val Gly Ala Ala Thr 130 135 140

Val Gly Gln Met Phe Thr Phe Gln Pro Arg Arg His Trp Thr Thr Gln 165 170 175

Asp Cys Asn Cys Ser Ile Tyr Thr Gly His Ile Thr Gly His Arg Met 180 185 190

Ala

#### (2) INFORMATION FOR SEQ ID NO: 169:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 579 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: NO
- (iii) ANTI-SENSE: NO
- (ix) FEATURE:
  - (A) NAME/KEY: CDS
  - (B) LOCATION: 1..579
- (ix) FEATURE:
  - (A) NAME/KEY: mat_peptide
  - (B) LOCATION: 1..576

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 169:

							GGA Gly								48
				_		_	CTG Leu 25								96
							GGG Gly								144
				_			TCG Ser							-	192
_	_						GGC Gly								240
							GAG Glu								288
							AAG Lys 105								336
							GCG Ala								384
		Pro					GAC Asp				Gly				432
	Cys				Val					Gly			TTG Leu 160		480
				Thr			Pro		Arg				CAG Gln		528
			Ser					His				Arg	ATG Met		576
GCT Ala															579

(2) INFORMATION FOR SEQ ID NO: 170:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 193 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (i1) MOLECULE TYPE: protein
- (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 170:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala 1 5 10 15

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val 20 25 30

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55 60

Gly Val Asn Tyr Arg Asn Ala Ser Gly Val Tyr His Ile Thr Asn Asp 65 70 75 80

Cys Pro Asn Ala Ser Ile Val Tyr Glu Thr Asp Asn His Ile Leu His 85 90 95

Leu Pro Gly Cys Val Pro Cys Val Lys Thr Gly Asn Gln Ser Arg Cys
100 105 110

Trp Val Ala Leu Thr Pro Thr Val Ala Ser Pro Tyr Val Gly Ala Pro 115 120 125

Leu Glu Pro Leu Arg Arg His Val Asp Leu Met Val Gly Ala Ala Thr 130 135 140

Val Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys Gly Gly Leu Phe Leu 145 150 155 160

Val Gly Gln Met Phe Thr Phe Gln Pro Arg Arg His Trp Thr Thr Gln 165 170 175

Asp Cys Asn Cys Ser Ile Tyr Ala Gly His Ile Thr Gly His Arg Met 180 185 190

Ala

- (2) INFORMATION FOR SEQ ID NO: 171:
  - (1) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 579 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA

(1111)	HYPOTHETICAL:	NO
(111)	HIPOIREILCAL:	NU

(ili) ANTI-SENSE: NO

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 1..579

(ix) FEATURE:

(A) NAME/KEY: mat_peptide

(B) LOCATION: 1..576

### (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 171:

			GAC Asp								-	48
			GCC Ala									96
			TAT Tyr									144
			GCA Ala									192
			AAC Asn 70									240
			ATA Ile									288
			CCT Pro									336
			CCC							CCA Pro		384
	Ser							Gly		AĊA Thr		432
							Gly			CTA Leu 160		430
			Thr			Leu				CAG Gln		528

GAG TGC AAT TGT TCC ACC TAT CCG GGC CAC ATC ACG GGT CAT AGA ATG
Glu Cys Asn Cys Ser Thr Tyr Pro Gly His Ile Thr Gly His Arg Met
180 185 190

GCG S79

- (2) INFORMATION FOR SEQ ID NO: 172:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 193 amino acids
    - (B) TYPE: amino acid
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 172:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala

1 10 15

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val
20 25 30

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe
35 40 45

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55 60

Ala Val His Tyr His Asn Thr Ser Gly Ile Tyr His Leu Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Phe Glu Ala Val His His Ile Leu His 85 90 95

Leu Pro Gly Cys Val Pro Cys Val Arg Thr Gly Asn Gln Ser Arg Cys 100 105 110

Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Pro Tyr Leu Gly Ala Pro 115 120 125

Leu Glu Ser Met Arg Arg His Val Asp Leu Met Val Gly Thr Ala Thr 130 140

Leu Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys Gly Gly Ile Phe Leu 145 150 155 160

Ala Gly Gln Met Phe Thr Phe Arg Pro Arg Leu His Trp Thr Thr Gln 165 170 175

Glu Cys Asn Cys Ser Thr Tyr Pro Gly His Ile Thr Gly His Arg Met 180 185 190

Ala

(2)	INF	ORMA:	rion	FOR	SEQ	ID i	NO: 3	173:								
	(i)	() ()	QUENC A) La B) TY C) ST C) TC	engti CPE : CRANI	i: 51 nucl	79 ba Leic ESS:	ase p acid	pair:	5							
	(ii)	MOI	LECUI	LE T	PE:	CDN	¥.									
	(iii)	HYI	POTHE	TIC	L: N	10										
	(iii)	ANT	ri-se	ENSE :	NO											
		() (E FE) ()	ATURE A) NA B) LO ATURE A) NA B) LO	AME/F DCATI E: AME/F	ON:	15	_pept	side								-
	(xi)	SEC	QUENC	CE DE	ESCRI	PTIC	ON: S	SEQ :	ID NO	): 17	73:					
ACG Thr 1	TGC Cys	GGT Gly	TCC Ser	GCC Ala 5	GAC Asp	CTC Leu	ATG Met	GGA Gly	TAC Tyr 10	ATC Ile	CCG Pro	CTC Leu	GTA Val	GGC Gly 15	GCC Ala	48
CCT Pro	GTG Val	GGT Gly	GGC Gly 20	GTC Val	GCC Ala	AGG Arg	GCC Ala	TTG Leu 25	GCG Ala	CAT His	GGC Gly	GTC Val	AGG Arg 30	GCT Ala	GTG Val	96
			ATA Ile													144
			CTT Leu													192
			TAT Tyr													240
			TCT Ser													288
			TGC Cys 100													336

Trp Ile Ala Leu Thr Pro Thr Leu Ala Ala Pro His Ile Gly Ala Pro

TGG ATA GCC TTG ACC CCT ACG TTG GCC GCG CCA CAC ATT GGC GCT CCA 384

	115					120					125				
CTT GAG Leu Glu 130	Ser	ATG Met	CGA Arg	Arg	CAT His 135	GTG Val	GAT Asp	TTG Leu	ATG Met	GTA Val 140	GGC Gly	ACT Thr	GCC Ala	ACA Thr	432
TTG TGC Leu Cys 145	TCC Ser	GCA Ala	CTC Leu	TAC Ty: 150	ATT Ile	GGA Gly	GAT Asp	CTG Leu	TGC Cys 155	GGA Gly	GGC Gly	ATA Ile	TTT Phe	CTA Leu 160	480
GTG GGC Val Gly	CAG .	ATG Met	TTC Phe 165	AAC Asn	TTC Phe	AGG Arg	Pro CCC	CGC Arg 170	CTG Leu	CAC His	TGG Trp	ACC Thr	ACC Thr 175	CAG Gln	528
GAG TGC Glu Cys	Asn	TGT Cys 180	TCC Ser	ATC Ile	TAT Tyr	CCA Pro	GGC Gly 185	CAC His	ATC Ile	ACG Thr	GGT Gly	CAC His 190	AGA Arg	ATG Met	576
GCG Ala														-	579

# (2) INFORMATION FOR SEQ ID NO: 174:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 193 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 174:

Thr Cys Gly Ser Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala
1 5

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val 20 25 30

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55 60

Ala Val His Tyr His Asn Thr Ser Gly Ile Tyr His Ile Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Phe Glu Ala Glu His His Ile Leu His

Leu Pro Gly Cys Val Pro Cys Val Arg Thr Gly Asn Gln Ser Arg Cys
100 105 110

Trp Ile Ala Leu Thr Pro Thr Leu Ala Ala Pro His Ile Gly Ala Pro 115 120 125

Leu	Glu 130	Ser	Mec	Arg	Arg	His 135	Val	Asp	Leu	Met	Val 140	Gly '	Thr	Ala	Thr	
Leu 145	Cys	Ser	Ala	Leu	Tyr 150	Ile	Gly	Asp	Leu	Cys 155	Gly	Gly	Ile		Leu 160	
Val	Gly	Gln	Mes	Phe 165	Asn	Phe	Arg	Pro	Arg 170	Leu	Hıs	Trp		Thr 175	Gln	
Glu	Cys	Asn	Cys 180	Ser	Ile	Tyr	Pro	Gly 185	Ħis	Ile	Thr	-	His 190	Arg	Met	
Ala																
(2)	INF	ORMA:	rion	FOR	SEQ	ID N	10: I	L75:								
	(±)	() ()	QUENC A) LE B) TY C) SI D) TO	NGTI PE: RANI	H: 57 nucl	9 ba .eic ESS:	acio sing	pair i	s							-
	(11	) MO	LECUI	E T	YPE:	CDN	A.									
	(iii	) HY	POTHE	TIC	AL: 1	10										
	(iii	) AN	TI-SE	ENSE	: NO											
	(ix	(	ATURI A) Ni B) Lo	ME/			579									
	(1x	(	ATURI A) Ni B) Lo	AME/				tide	<b>:</b>							
	(xi	) SE	QUEN	CE D	ESCR	IPTI	ON:	SEQ	ID 1	<del>1</del> 0: 1	.75 :					
	Cys		TTT Phe		qaA .					: Ile					Ala	48
			GGC Gly 20	Val					ı Al					Ala	GTG Val	96
			/ Ile					Gl;					Cys		TTT Phe	144
		TTC Phe	CTT				CTC	TC				GTC Val	. cc		TCG Ser	192
GC	G CAG	G CAG	C TAC	CGG	AA C	TA	TC	G GG	C AT	T TA	T CAG	GTO	acc	: AA:	GAC	240

Ala Gln His Tyr Arg Asn Ile Ser Gly Ile Tyr His Val Thr Asn Asp

65			<b>7</b> 0			75			80		
				GTG Val						-	288
				TGC Cys							336
				ACT Thr							384
				CAC His 135							432
				ATC Ile						-	480
				TTC Phe							528
				TAT Tyr							576
GCT Ala											579

- (2) INFORMATION FOR SEQ ID NO: 176:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 193 amino acids
    - (B) TYPE: amino acid
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 176:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala
1 5 10 15 .

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val 20 25 30

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55 60

								22	6							
Ala 65	Gln	His	Tyr	Arg	Asn 70	Ile	Ser	Gly	Ile	Tyr 75	His	Val	Thr	Asn	Asp 80	
Суѕ	Pro	Asn	Ser	Ser '85	Ile	Val	Tyr	Glu	Ala 90	Asp	His	His	Ile	Met 95	His	
Leu	Pro	Gly	Cys 100	Val	Pro	Cys	Val	Arg 105	Thr	Gly	Asn	Thr	Ser 110	Arg	Cys	
Trp	Val	Pro 115	Leu	Thr	Pro	Thr	Val 120	Ala	Ala	Pro	Tyr	<b>Val</b> 125	Gly	Ala	Pro	
Leu	Glu 130	Ser	Met	Arg	Аrg	H15 135	۷al	Asp	Leu	Met	Val 140	Gly	Ala	Ala	Thr	
Val 145	Cys	Ser	Ala	Leu	Туг 150	Ile	Gly	Asp	Leu	Cys 155	Gly	Gly	Val	Phe	Leu 160	
Val	Gly	Gln	Met	Phe 165	Thr	Phe	Arg	Pro	Arg 170	Arg	His	Trp	Thr	Thr 175	Gln .	
Asp	Cys	Asn	Cys 180	Ser	Ile	Tyr	Asp	Gly 185	His	Ile	Thr	Gly	His 190	Arg	Met	
Ala																
(2)	INFO	ORMA?	rion	FOR	SEQ	ID :	NO: 1	177:								
	(i)	(2 (1	QUENC A) LE B) TY C) ST D) TC	engti (PE : TRANI	f: 57 nucl	79 ba Leic ESS:	ase p acid	pairs 1	3							
	(ii)	MOI	LECUI	LE T	PE:	CDN	Ą									
1	(iii)	HYI	POTHE	ETIC	AL: 1	10										
,	(iii)	AN.	rı-sı	ENSE	: <b>N</b> O											

- (ix) FEATURE:
  - (A) NAME/KEY: CDS
  - (B) LOCATION: 1..579
- (ix) FEATURE:
  - (A) NAME/KEY: mat_peptide
  - (B) LOCATION: 1..576
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 177:

ACG TGC GGG TTC GCC GAC CTC ATG GGA TAC ATC CCG CTC GTG GGC GCT 48 Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala

CCA GTA GGA GGC GTC GCC AGA GCC TTG GCG CAT GGC GTC AGG GCT GTG Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val

GCC Ala

								227	7								
			20					25					30				
				AAT Asn												144	
				TTG Leu			Leu									192	
				CGG Arg												240	
				AGT Ser 85												288	
				GTG Val												⁻ 336	
				ACA Thr												384	
		Ser		CGG Arg								Gly				432	•
	Cys					Ile					Gly				TTG Leu 160	480	)
					Ser					J Arg					CAG Gln	529	3
GA1 Asj	r TGC p Cys	AAC Asi	TG1 Cys	s Ser	ATC	TAT Tyr	GTC Val	G GGC L Gl ₁ 185	/ His	C ATO	Thi	GGC Gly	CAC His	Arc	ATG Met	57	5

# (2) INFORMATION FOR SEQ ID NO: 178:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 193 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 178:

- Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala
  1 5 10 15
- Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val 20 25 30
- Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe
  35 40 45
- Ser Ile Phe Leu Leu Val Leu Leu Ser Arg Leu Thr Val Pro Ala Ser 50 55 60
- Ala Gln His Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp 65 70 75 80
- Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp His His Ile Met His
  85 90 95
- Leu Pro Gly Cys Val Pro Cys Val Arg Thr Gly Asn Val Ser Arg Cys 100 105 110
- Trp Ile Pro Leu Thr Pro Thr Val Ala Val Pro Tyr Leu Gly Ala Pro 115 120 125
- Leu Thr Ser Val Arg Gln His Val Asp Leu Met Val Gly Ala Ala Thr 130 135 140
- Leu Cys Ser Ala Leu Tyr Ile Gly Asp His Cys Gly Gly Val Phe Leu 145 150 155 160
- Ala Gly Gln Met Val Ser Phe Gln Pro Arg Arg His Trp Thr Thr Gln 165 170 175
- Asp Cys Asn Cys Ser Ile Tyr Val Gly His Ile Thr Gly His Arg Met 180 185 190

Ala

- (2) INFORMATION FOR SEQ ID NO: 179:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 579 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: NO
  - (ix) FEATURE:
    - (A) NAME/KEY: CDS
    - (B) LOCATION: 1..579

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17	(xi)	SEQUENCE	DESCRIPTION:	SEO	ID	NO:	179
------------------------------------------	------	----------	--------------	-----	----	-----	-----

ACCTGCGGCT	TCGCCGACCT	CATGGGATAC	ATCCCGCTCG	TAGGCGCCCC	CGTGGGAGGC	60
GTCGCCAGAR	CTCTGGCGCA	TGGCGTCAGG	GCTCTGGAAG	ACGGGATCAA	TTATGCAACA	120
GGGAATCTTC	CTGGTTGCTC	TTTCTCTATC	TCCCTTCTTG	AACTTCTCTC	GTGCCTGACT	180
GTTCCCGCCT	CAGCCATCCA	CTATCGCAAT	GCTTCGGACG	GTTATTATAT	CACCAATGAT	240
TGCCCGAACT	CTAGCATAGT	GTATGAAGCC	GAGAACCACA	TCTTGCACCT	TCCGGGGTGT	300
ATACCCTGTG	TGAAGACCGG	GAATCAGTCG	CGGTGCTGGG	TGGCTCTCAC	CCCCACGCTG	360
GCGGCCCCAC	ACCTACGTGC	TCCGCTTTCG	TCCTTACGGG	CGCATGTGGA	CCTAATGGTG	420
GGGGCCGCCA	CGGCATGCTC	CGCTTTTTAC	ATTGGAGATC	TGTGCGGGGG	TGTGTTTTTG	480
GCGGGCCAAC	TGTTCACTAT	CCGGCCACGC	ATTCATGAAA	CCACTCAGGA	CTGCAATTGC	540
TCCATCTACT	CAGGGCACAT	CACGGGTNNN	NNNNNNNNN			579

# (2) INFORMATION FOR SEQ ID NO: 180:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 193 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 180: Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala
- Pro Val Gly Gly Val Ala Arg Xaa Leu Ala His Gly Val Arg Ala Leu 20 25 30
- Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45
- Ser Ile Ser Leu Leu Glu Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55 60
- Ala Ile His Tyr Arg Asn Ala Ser Asp Gly Tyr Tyr Ile Thr Asn Asp 65 70 75 80
- Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Glu Asn His Ile Leu His 85 90 95
- Leu Pro Gly Cys Ile Pro Cys Val Lys Thr Gly Asn Gln Ser Arg Cys
  100 105 110

(2)

420

480

230

Trp	Val	Ala 115	Leu	Thr	Pro	Thr	Leu 120	Ala	Ala	Pro	His	Leu 125	Arg	Ala	Pro	
Leu	Ser 130	Ser	Leu	Arg	Ala	His 135	Val	Asp	Leu	Met	Val 140	Gly	Ala	Ala	Thr	
Ala 145	Cys	Ser	Aia	Phe	Tyr 150	Ile	Gly	Asp	Leu	Cys 155	Gly	Gly	Val	Phe	Leu 160	
Ala	Gly	Gln	Leu	Phe 165	Thr	Ile	Arg	Pro	<b>Arg</b> 170	Ile	His	Glu	Thr	Thr 175	Gln	
Asp	Суз	Asn	Cys 180	Ser	Ile	Tyr	Ser	Gly 185	His	Ile	Thr	Gly	Xaa 190	Xaa	Xaa	
Хаа	/														-	-
(2) INFO	RMAT:	ION :	FOR	SEQ :	ID N	0: 1:	81:									
(i)	(B (C	) LE ) TY ) ST	ngth PE : Rand	ARAC' : 57: nucl: EDNE: GY:	9 ba eic SS:	se p acid sing	airs									
(ii)	MOL	ECUL	Z TY	PE:	CDNA											
(iii)	HYP	OTHE	TICA	L: N	0											
(iii)	ANT	I-SE	NSE:	NO												
(ix)		AN (.	ME/K	EY:		i78										
(xi)	SEC	UENC	E DE	ESCRI	PTIC	N: S	EQ :	ID NO	): 18	31:						
GCGTGCGG	cr 1	cgcc	CGATO	CT CA	\TGG(	SATAC	E AT	cccc	TCG	TAG	ECGC	ccc (	CGTG	GTG	3C	60
GTCGCCAC	GAG C	CCTC	GCG	LA CO	GTG	TTAGO	G GC	TGTG	GAGG	ACG	GGAT	TAA	CTAC	GCAA	CA	120
GGGAATC	rrc d	TGG1	rrge:	rc Ti	TCT	CTATO	TN	CCTT	CTGG	CAC'	TTCT	CTC	GTGC	CTGA	CT	180
GTCCCGG	cr o	GGC1	rcago	CA CT	racc	GGAA?	r GT	CTCG	GGCA	TCT	ACCA:	CGT	CACC	AATG	AT	240
TGCCCGA	ATT (	CAG	CATAC	GT G	ratg.	AAGC	C GA	TCAC	CACA	TCA	TGCA	CTT	ACCA	GGGT	GC	300
אידארירירייי		רבא ריני ייים איריני	3 A C C (	aa a:	2206	الملتك	ۍ رو	СТСС	TCCC	TAT	СТСТ	GAC	ACCT	ACTG	TG	360

GCTGCTCCCT ACCTCGGGGC TCCGCTTACG TCGCTACGGC GGCATGTGGA TTTGATGGTG

GGTGCAGCCA CCCTTTGCTC TGCCCTCTAC GTCGGAGACC TCTGTGGAGG TGTCTTCCTA

GTGGGACAGA TGTTCACCTT CCAGCCGCGC CGCCACTGGA CCACTCAGGA CTGCAACTGC 540

TCCATTTACG TCGGCCACAT CACAGGCCAC AGAATGGCT 579

- (2) INFORMATION FOR SEQ ID NO: 182:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 193 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 182:
  - Ala Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala 1 5 10 15
  - Pro Val Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val
  - Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45
  - Ser Ile Xaa Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55 60
  - Ala Gln His Tyr Arg Asn Val Ser Gly Ile Tyr His Val Thr Asn Asp 65 70 75 80
  - Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp His His Ile Met His 90 95
  - Leu Pro Gly Cys Ile Pro Cys Val Arg Thr Gly Asm Val Ser Arg Cys 100 105 110
  - Trp Val Ser Leu Thr Pro Thr Val Ala Ala Pro Tyr Leu Gly Ala Pro 115 120 125
  - Leu Thr Ser Leu Arg Arg His Val Asp Leu Met Val Gly Ala Ala Thr 130 135 140
  - Leu Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys Gly Gly Val Phe Leu 145 150 155 160
  - Val Gly Gln Met Phe Thr Phe Gln Pro Arg Arg His Trp Thr Thr Gln 165 170 175
  - Asp Cys Asn Cys Ser Ile Tyr Val Gly His Ile Thr Gly His Arg Met 180 185 190

Ala

(2)	INFORMATION	FOR	SEO	ID	NO:	183.

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 579 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: CDNA
- (ili) HYPOTHETICAL: NO
- (iii) ANTI-SENSE: NO
  - (1x) FEATURE:
    - (A) NAME/KEY: CDS
    - (B) LOCATION: 1..579
- (ix) FEATURE:
  - (A) NAME/KEY: mat_peptide
  - (B) LOCATION: 1..579
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 183:

ACC	TGC	GGC	TTT	GCC	GAC	CIC	ATG	GGA	TAC	ATC	CCG	CTC	GTA	GGC	GCC	48
Thr	Cys	Gly	Phe	Ala	Asp	Leu	Met	Gly	Tyr	Ile	Pro	Leu	Val	Gly	Ala	
1				5					10					15		

- CCT GTG GGT GGC GTC GCC AGG GCC CTA GAA CAC GGT GTT AGG GCT GTG

  Pro Val Gly Val Ala Arg Ala Leu Glu His Gly Val Arg Ala Val

  20

  25

  30
- GAG GAC GGT ATT AAT TAT GCA ACA GGG AAT CTC CCC GGT TGC TCT TTT

  Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe

  35

  40

  45
- TCT ATC TCC CTC TTG GCA CTT CTT TCG TGC CTG ACT GTT CCC ACC TCA

  Ser Ile Ser Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Thr Ser

  50 55 60
- GCC GTC AAC TAT CGC AAC GCC TCG GGC GTC TAT CAT ATC ACC AAT GAC
  Ala Val Asn Tyr Arg Asn Ala Ser Gly Val Tyr His Ile Thr Asn Asp
  65 70 75 80
- TGC CCG AAT TCG AGC ATA GTG TAC GAG GCT GAC TAC CAC ATC CTA CAC

  Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Tyr His Ile Leu His

  85

  90

  95
- CTC CCT GGG TGC TTA CCC TGC GTG AGG GTT GGG AAT CAG TCA CGC TGC

  Leu Pro Gly Cys Leu Pro Cys Val Arg Val Gly Asn Gln Ser Arg Cys

  100 105 110
- TGG GTG GCC CTT ACT CCC ACC GTG GCG GCG CCT TAC GTT GGT GCT CCG

  Trp Val Ala Leu Thr Pro Thr Val Ala Ala Pro Tyr Val Gly Ala Pro

	115			120			125			
		CTC Leu								432
		GCT Ala								480
		ATG Met								528
		TGT Cys 180								576
GCA Ala									-	<b>5</b> 79

- (2) INFORMATION FOR SEQ ID NC: 184:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 193 amino acids
    - (B) TYPE: amino acid
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 184:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Thr Ser 50 55 60

Ala Val Asn Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile Thr Asn Asp
65 70 75 80

Cys Pro Asn Ala Ser Ile Val Tyr Glu Thr Glu Asn His Ile Leu His
85 90 95

Leu Pro Gly Cys Val Pro Cys Val Arg Thr Gly Asn Gln Ser Arg Cys
100 105 110

Trp Val Ala Leu Thr Pro Thr Val Ala Ser Pro Tyr Ala Gly Ala Pro 115 120 125

Leu Glu Pro Leu Arg Arg His Val Asp Leu Met Val Gly Ala Ala Thr 130 135 140 Met Cys Ser Ala Leu Tyr Ile Gly Asp Leu Cys Gly Gly Leu Phe Leu 145 150 155 160

Val Gly Gln Met Phe Thr Phe Gln Pro Arg Arg His Trp Thr Thr Gln 165 170 175

Asp Cys Asn Cys Ser Ile Tyr Thr Gly His Ile Thr Gly His Arg Met 180 185 190

Ala

- (2) INFORMATION FOR SEQ ID NO: 182:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 192 amino acids
    - (B) TYPE: amino acid
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 182:

Ala Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala 1 5 10 15

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val 20 25 30

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

Ser Ile Ser Phe Trp His Phe Ser Arg Ala * Leu Ser Arg Pro Arg 50 55 60

Leu Ser Thr Thr Gly Met Ser Arg Ala Ser Thr Thr Ser Pro Met Ile
65 70 75 80

Ala Arg Ile Pro Ala * Cys Met Lys Pro Ile Thr Thr Ser Cys Thr 85 90 95

Tyr Gln Gly Ala Tyr Pro Ala * Gly Pro Gly Thr Phe Arg Ala Ala 100 105 110

Gly Tyr Leu * His Leu Leu Trp Leu Leu Pro Thr Ser Gly Leu Arg

Leu Arg Arg Tyr Gly Gly Met Trp Ile * Trp Trp Val Gln Pro Pro 130 135 140

Phe Ala Leu Pro Ser Thr Ser Glu Thr Ser Val Glu Val Ser Ser + 145 150 155 160

Trp Asp Arg Cys Ser Pro Ser Ser Arg Ala Ala Thr Gly Pro Leu Arg

Thr Ala Thr Ala Pro Phe Thr Ser Ala Thr Ser Gln Ala Thr Glu Trp

336

								23:	5							
		:	180				:	185				:	190			
(2) 1	INFO	RMAT:	ION :	FCR :	SEQ :	ID NO	): 1	85:								
	(i)	(A (B (C	UENC: ) LE ) TY: ) ST: ) TO	ngth PE: Rand	: 57: nucl EDNE:	9 ba: eic : SS: :	se pa acid sing	airs								
ı	(ii)	MOL	ECUL	E TY	PE:	cdna										
(3	Lii)	HYP	OTHE	TICA	L: N	0										
(:	iii)	ANT	I-SE	NSE:	NO											
		(A (B FEA (A	TURE ) NA ) LO .TURE	ME/K CATI : : ME/K	ON:	15 mat_	pept	ıde								-
	(xi)	SEC	UENC	E DE	SCRI	PTIC	N: 5	EQ I	D NO	): 18	15:					
ACT Thr 1																48
CCC Pro																96
GAG Glu																144
TCT Ser	ATC Ile 50	TAC Tyr	CTC Leu	TTG Leu	GCA Ala	CTT Leu 55	CTC Leu	TCG Ser	TGC <b>C</b> ys	CTG Leu	ACT Thr 60	GTT Val	CCC	ACC Thr	TCG Ser	192
			TAT Tyr			Ala					His					240
TGC	ÇCG	AAC	TCG	AGC	ATA	GTG	TAC	GAG	GCC	GAC	CAC	CAC	ATC	CTA	CAC	288

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp His His Ile Leu His

CTT CCA GGG TGC TTA CCC TGT GTG AGG GTT GGG AAT CAG TCA CGT TGT Leu Pro Gly Cys Leu Pro Cys Val Arg Val Gly Asn Gln Ser Arg Cys 105

90

TGG GTG GCC CTC TCT CCC ACC GTG GCG GCG CCT TAC ATC GGT GCT CCA 384

Trp	Val	Ala 115	Leu	Ser	Pro	Thr	Val 120	Ala	Ala	Pro	Tyr	Ile 125	Gly	Ala	Pro	
					AGA										-	432
GTG Val 145																480
GTT Val					TCT Ser											528
					ATC Ile											576 -
GCA Ala																579

- (2) INFORMATION FOR SEQ ID NO: 186:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 193 amino acids
    - (B) TYPE: amino acid
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 186:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala

Pro Val Gly Gly Val Ala Arg Ala Leu Glu His Gly Val Arg Ala Val
20 25 30

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe

Ser Ile Tyr Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Thr Ser 50 55

Ala Ile His Tyr Arg Asn Ala Ser Gly Val Tyr His Val Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp His His Ile Leu His
85 90 95

Leu Pro Gly Cys Leu Pro Cys Val Arg Val Gly Asn Gln Ser Arg Cys
100 -105 110

Trp Val Ala Leu Ser Pro Thr Val Ala Ala Pro Tyr Ile Gly Ala Pro 115 120 125

240

			23/	/			
Val Glu Se 130	er Phe Arg	Arg His V	Val Asp M		Val Gly 140	Ala Ala	Thr
Val Cys Se 145	er Ala Leu	Tyr Ile (	Gly Asp L	eu Cys 155	Gly Gly	Val Phe	Leu 160
Val Gly G	in Met Phe 165			Arg Arg	His Trp	Thr Thr 175	Gln
Asp Cys As	sn Cys Ser 180	Ile Tyr	Ala Gly B 185	His Ile	Thr Gly	His Gly 190	Мес
Ala							
(2) INFORM	ation for	SEQ ID NO	0: 187:				
(i) S	(B) TYPE: (C) STRAN	HARACTERIS H: 579 bas nucleic a DEDNESS: S CGY: linea	se pairs acid single				•
(ii) N	OLECULE T	YPE: cDNA					
(iii) F	YPOTHETIC	AL: NO					
(iii) <i>I</i>	NTI-SENSE	: NO					
(ix) I	FEATURE: (A) NAME/ (B) LOCAT	KEY: CDS	79				
(ix) I		KEY: mat_; TON: 15					
(xi) \$	SEQUENCE D	ESCRIPTION	N: SEQ II	NO: 18	7:		
ACT TGC GG Thr Cys Gi		Asp Leu					
CCT GTG GG							
GAG GAC GG Glu Asp G							
TCT ATC T Ser Ile P							

GCC GTC AAC TAT CGC AAT GCC TCG GGC ATC TAT CAC ATC ACC AAT GAC

Ala 65	Val	Asn	Tyr	Arg	Asn 70	Ala	Ser	Gly	Ile	Tyr 75	His	Ile	Thr	Asn	Asp 80		
					ATA Ile												283
					520 CCC												336
					D.O.												384
					AGT Ser											•	432
					TAC Tyr 150												480
					TCT Ser												528
					ATC				H:s						ATG Met		576
GCA Ala																	579

- (2) INFORMATION FOR SEQ ID NO: 188:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 193 amino acids
    - (B) TYPE: amino acid
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 188:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala 1 5 10

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val 20 25 30

Glu Asp Gly Ile Asn Tyr Ala Thr-Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Thr Ser 50 60

Ala Val Asn Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Thr Glu His His Ile Leu His
85
90
95

Leu Pro Gly Cys Leu Pro Cys Val Arg Val Gly Asn Gln Ser Arg Cys
100 105 110

Trp Val Ala Leu Thr Pro Thr Val Ala Ala Pro Tyr Ile Gly Ala Pro 115 120 125

Leu Glu Ser Leu Arg Ser His Val Asp Leu Met Val Gly Ala Ala Thr 130 135 140

Ala Cys Ser Ala Leu Tyr Ile Gly Asp Leu Cys Gly Gly Val Phe Leu 145 150 155 160

Val Gly Gln Met Phe Ser Phe Gln Pro Arg Arg His Trp Thr Thr Gln 165 170 175

Asp Cys Asn Cys Ser Ile Tyr Ala Gly His Val Thr Gly His Arg Met 180 185 190

Ala

- (2) INFORMATION FOR SEQ ID NO: 189:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 579 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: NO
  - (ix) FEATURE:
    - (A) NAME/KEY: CDS
    - (B) LOCATION: 1..579
  - (ix) FEATURE:
    - (A) NAME/KEY: mat_peptide
    - (B) LOCATION: 1..576
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 189:

ACG TGC GGC TTC GCC GAC CTC ATG GGA TAC ATC CCG CTC GTG GGC GCC

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala

1 10 15

								_									
CCC Pro	GTT Val	GGG Gly	GGC Gly 20	GTC Val	GCC Ala	AGG Arg	GCC Ala	CTG Leu 25	GCG Ala	CAT His	GGC Gly	GTC Val	AGG Arg 30	GCT Ala	GTG Val		96
GAG Glu	GAC Asp	GGG Gly 35	ATT Ile	AAC Asn	TAT Tyr	GCG Ala	ACA Thr 40	GGG Gly	AAT Asn	CTT Leu	CCC	GGT Gly 45	TGC Cys	TCT Ser	TTC Phe		144
TCT Ser	ATC Ile 50	TTC Phe	CTC Leu	CTG Leu	GCA Ala	CTT Leu 55	CTT Leu	TCG Ser	TGC Cys	CTC Leu	ACT Thr 60	GTC Val	CCA Pro	GCG Ala	TCA Ser		192
GCT Ala 65	GAG Glu	CAC H1s	TAC Tyr	CGG Arg	AAT Asn 70	GCT Ala	TCG Ser	GGC Gly	ATC Ile	TAT Tyr 75	CAC His	ATC Ile	ACC Thr	AAT Asn	GAC Asp 80		240
TGT Cys	CCG Pro	AAT Asn	TCC Ser	AGC Ser 85	GTA Val	GTC Val	TAT Tyr	GAA Glu	ACT Thr 90	GAC Asp	CAC H1s	CAT Hls	ATA Ile	TTG Leu 95	CAC H1s	-	288
TTG Leu	CCG Pro	GGG Gly	TGC Cys 100	GTA Val	CCC	TGC Cys	GTG Val	AGG Arg 105	GCC Ala	GGG Gly	AAC Asn	GTG Val	TCT Ser	CGT Arg	TGC Cys		336
TGG Trp	ACG Thr	CCG Pro	GTA Val	ACA Thr	CCT Pro	ACG Thr	GTG Val 120	GCT Ala	GCC Ala	GTA Val	TCC Ser	ATG Met	GAC Asp	GCT Ala	CCG Pro		384
					CGG Arg							GGT					432
GTG Val 145	TGT Cys	TCT Ser	GTC Val	CTC Leu	TAT Tyr 150	GTT Val	GGA Gly	GAC Asp	CTC Leu	TGT Cys 155	GGA Gly	GGT Gly	GCT Ala	TTC Phe	CTA Leu 160		480
					ACC Thr										CAG		528
					ATC Ile									AGG			576
GCG Ala																	579

# (2) INFORMATION FOR SEQ ID NO: 190:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 193 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (11) MOLECULE TYPE: protein

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 190:
- Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala 1 5 10 15
- Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val 20 25 30
- Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45
- Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55 60
- Ala Glu His Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile Thr Asn Asp 65 70 75 80
- Cys Pro Asn Ser Ser Val Val Tyr Glu Thr Asp His His Ile Leu His 85 90 95
- Leu Pro Gly Cys Val Pro Cys Val Arg Ala Gly Asn Val Ser Arg Cys
  100 105 110
- Trp Thr Pro Val Thr Pro Thr Val Ala Ala Val Ser Met Asp Ala Pro 115 120 125
- Leu Glu Ser Phe Arg Arg His Val Asp Leu Met Val Gly Ala Ala Thr 130 135 140
- Val Cys Ser Val Leu Tyr Val Gly Asp Leu Cys Gly Gly Ala Phe Leu 145 150 155 160
- Val Gly Gln Met Phe Thr Phe Gln Pro Arg Arg His Trp Thr Thr Gln 165 170 175
- Asp Cys Asn Cys Ser Ile Tyr Thr Gly His Ile Thr Gly His Arg Met 180 185 190

Ala

- (2) INFORMATION FOR SEQ ID NO: 191:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 289 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: NO
  - (ix) FEATURE:
    - (A) NAME/KEY: CDS

(B)	LOCA	: NOIT	1	289

#### (ix) FEATURE:

- (A) NAME/KEY: mat_peptide
- (B) LOCATION: 1..286

# (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 191:

ATG Met 1	AGC Ser	ACG Thr	AAT Asn	CCT Pro 5	AAA Lys	CCT Pro	CAA Gln	AGA Arg	AAA Lys 10	ACC Thr	AAA Lys	CGT Arg	AAC Asn	ACC Thr 15	AAC Asn			48
CGC Arg	CGC Arg	CCC Pro	ATG Met 20	GAC Asp	GTT Val	AAG Lys	TTC Phe	CCG Pro 25	GGC Gly	GGT Gly	GGC Gly	CAG Gln	ATC Ile 30	GTT Val	GGT Gly			96
GGA Gly	GTT Val	TAC Tyr 35	TTG Leu	TTG Leu	CCG Pro	CGC Arg	AGG Arg 40	GGC Gly	Pro CCC	AGG Arg	TTG Leu	GGT Gly 45	GTG Val	yrg	GCG Ala		-	144
ACT Thr	AGG Arg 50	AAG Lys	ACT Thr	TCG Ser	GAG Glu	CGG Arg 55	TCG Ser	CAA Gln	CCT Pro	CGT Arg	GGG Gly 60	AGA Arg	CGT Arg	CAG Gln	CCT Pro			192
ATC Ile 65	CCC Pro	AAG Lys	GCA Ala	CGT Arg	CGA Arg 70	TCT Ser	GAG Glu	GGA Gly	AGG Arg	TCC Ser 75	TGG Trp	GCT Ala	CAG Gln	CCC Pro	GGG Gly 80			240
TAC Tyr	CCA Pro	TGG Trp	CCT Pro	CTT Leu 85	TAC Tyr	GGT Gly	AAT Asn	GAG Glu	GGT Gly 90	TGT Cys	GGG Gly	TGG Trp	GCA Ala	GGA Gly 95	TGG Trp	G		289

# (2) INFORMATION FOR SEQ ID NO: 192:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 96 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 192:

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn 1 5 10 15

Arg Arg Pro Met Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly

Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala

Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro 50 55 60

Ile Pro Lys Ala Arg Arg Ser Glu Gly Arg Ser Trp Ala Gln Pro Gly

65		7	0				75					80		
Tyr Pro	Trp Pro	Leu Ty 85	r Gly	Asn (	Glu (	31y ( 90	Cys (	Gly 7	(rp	Ala (	3ly ' 95	Trp		
(2) INFO	RMATION	FOR SE	EQ ID N	0: 19	93:									
(i)	(B) TY (C) SI	NGTH: PE: nu RANDEL	RACTERI 498 ba icleic ONESS: 7: line	se pa acid singl	airs									
(ii)	MOLECUI	LE TYPE	E: cDNA											
(iii)	нуротна	ETICAL:	: NO										-	
(iii)	ANTI-SE	ENSE: 1	MO											
		AME/KET DCATION	Y: CDS N: 14	98										
(xi)		OCATIO	Y: mat_ N: 14	95		ם אוכ	): 19	33:						
	ACG AAT Thr Asn												48	
1	IIII ASII	5	ys Flo	GIII	<i>n</i> . 9	10	****	Буз	na 9	7.011	15			
	CCT ATG Pro Met 20	V qaA											96	
	TAC TTG												144	
Gry var	35	Leu P	TO ALG	40	GIY	110	Arg	nea	45	Val	AL 9	Aza		
	AAG ACT Lys Thr												192	
	AAG GCG Lys Ala							Trp					240	
	TGG CCC				C3.C		mm	ccc	mc-c	CCN	ccc	TGG	288	ı

Tyr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp

CTC CTG TCT CCT CGC GGC TCT CGG CCA TCT TGG GGC CCA AAT GAT CCC

90

Leu	Leu	Ser	Pro 100	Arg	Gly	Ser	Arg	Pro 105	Ser	Trp	Gly	Pro	Asn 110	Asp	Pro		
CGG Arg	CGG Arg	AGA Arg 115	TCG Ser	CGC Arg	AAT Asn	CTG Leu	GGT Gly 120	AAG Lys	GTC Val	ATC Ile	GAT Asp	ACC Thr 125	CTG Leu	ACG Thr	TGC Cys		384
GGC Gly	TTC Phe 130	GCC Ala	GAC Asp	CTC Leu	ATG Met	GGA Gly 135	TAC Tyr	ATC Ile	CCG Pro	CTC Leu	GTG Val 140	GGC Gly	GCC Ala	CCC Pro	GTC Val		432
GGG Gly 145	GGC Gly	GTC Val	GCC Ala	AGG Arg	GCC Ala 150	CTG Leu	GCG Ala	CAT Hıs	GGC Gly	GTC Val 155	AGG Arg	GCT Ala	GTG Val	GAG Glu	GAC Asp 160		480
GGG Gly																-	498

- (2) INFORMATION FOR SEQ ID NO: 194:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 166 amino acids
    - (B) TYPE: amino acid
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 194:

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn

1 5 10 15

Arg Arg Pro Met Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly 20 25 30

Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala 35 40 45

Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro
50 60

Ile Pro Lys Ala Arg Arg Ser Glu Gly Arg Ser Trp Ala Gln Ala Gly
65 70 75 80

Tyr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp 85 90 95

Leu Leu Ser Pro Arg Gly Ser Arg Pro Ser Trp Gly Pro Asn Asp Pro 100 105 110

Arg Arg Arg Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys 115 120 125

Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala Pro Val 130 140

Gly Gly Val Ala Arg Al 145 15		s Gly Val A	rg Ala Val Glu	Asp 160
Gly Ile Asn Tyr Arg Gl 165	n			
(2) INFORMATION FOR SE	Q ID NO: 195	i:		
(B) TYPE: nu	579 base pai cleic acid NESS: single	rs		
(ii) MOLECULE TYPE	: cDNA			
(iii) HYPOTHETICAL:	NO			-
(iii) ANTI-SENSE: N	0			
(1x) FEATURE: (A) NAME/KEY (B) LOCATION				
(B) LOCATION				
(xi) SEQUENCE DESC				
ACG TGC GGA TTC GCC GA Thr Cys Gly Phe Ala As				Gly
CCC GTT GGG GGC GTC GC				•
Pro Val Gly Gly Val Al	a Arg Ala Le		GGT GTG AGG GTT	CTT 96
Pro Val Gly Gly Val Al	a Arg Ala Le 2 AT GCA ACA GO	eu Ala His G 25 GG AAT CTG C	GGT GTG AGG GTT Gly Val Arg Val 30	C CTT 96 Leu
Pro Val Gly Gly Val Al 20 GAG GAC GGG GTG AAT TA Glu Asp Gly Val Asn Ty	AT GCA ACA GO TALA THE GLA AT GCA ACA GO TALA THE GLA AO TALA CTT CTC TO	eu Ala His G 25 GG AAT CTG C ly Asn Leu F CG TGC CTC A	GGT GTG AGG GTTGING VALUE ACT GGT TGC TCC GGT TGC TCC 45	C CTT 96 Leu C TTC 144 C Phe C TCT 192
Pro Val Gly Gly Val Al 20  GAG GAC GGG GTG AAT TA GLU Asp Gly Val Asn Ty 35  TCT ATC TTC ATT CTT GC Ser Ile Phe Ile Leu Al 50  GCA GTT CCC TAC CGA AA Ala Val Pro Tyr Arg As	AT GCA ACA GC AT ALA Thr GI 40 CA CTT CTC TC La Leu Leu Sc 55	eu Ala His G 25 GG AAT CTG C ly Asn Leu F CG TGC CTC F er Cys Leu 1	GGT GTG AGG GTTG Sly Val Arg Val 30 CCT GGT TGC TCT Pro Gly Cys Set 45 ACT GTC CCG GCC Thr Val Pro Als 60 CAT GTC ACC AA	F CTT 96 Leu  F TTC 144 F Phe  C TCT 192 A Ser  F GAT 240

GCA CCT GGC TGC GTG CCT TGT GTC AGG AAA GAT AAT GTG AGT AGG TGC 336

Ala	Pro	Gly	Cys 100	Val	Pro	Cys	Val	Arg 105	Lys	Asp	Asn	Val	Ser 110	Arg	Cys	
TGG Trp	GTC Val	CAA Gln 115	ATT Ile	ACC Thr	CCC Pro	ACG Thr	CTG Leu 120	TCA Ser	GCC Ala	CCG Pro	AGC Ser	TTC Phe 125	GGA Gly	GCA Ala	GTC Val	384
ACG Thr	GCT Ala 130	CCC Pro	CTT Leu	CGG Arg	AGA Arg	GCC Ala 135	GTT Val	GAT Asp	TAC Tyr	TTG Leu	GTG Val 140	GGA Glγ	GGG Gly	GCT Ala	GCC Ala	432
CTC Leu 145	TGC Cys	TCC Ser	GCG Ala	TTA Leu	TAC Tyr 150	GTT Val	GGA Gly	GAC Asp	GCG Ala	TGT Cys 155	GGG Gly	GCA Ala	CTA Leu	TTT Phe	TTG Leu 160	480
				TTC Phe 165												528
				TCC Ser											ATG Met	576
GCA Ala																579

#### (2) INFORMATION FOR SEQ ID NO: 196:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 193 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 196:

Thr Cys Gly Phe Ala Asp Leu Val Gly Tyr Ile Pro Leu Val Gly Gly
1 5 10 15

Pro Val Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu 20 25 30

Glu Asp Gly Val Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

Ser Ile Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 60

Ala Val Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Leu Ile Leu His
85 90 95

Ala Pro Gly Cys Val Pro Cys Val Arg Lys Asp Asn Val Ser Arg Cys
100 105 110

Trp	Val	Gln 115	Ile	Thr	Pro	Thr	Leu 120	Ser	Ala	Pro	o Se		Phe 125	Gly	Ala	Va	1		
Thr	Ala 130	Pro	Leu	Arg	Arg	Ala 135	Val	Asp	Tyr	Le	u Va 14		Gly	Gly	Ala	Al	a		
Leu 145	Cys	Ser	Ala	Leu	Ty= 150	Val	Gly	qeA	Ala	. Су 15		Ly i	Ala	Leu	Phe	Le 16	iu 10		
Val	Gly	Gln	Met	Phe 165	Thr	Tyr	Arg	Pro	Arg 170		n Hi	is.	Ala	Thr	Val 175	G1	.n		
Asp	Суз	Asn	Cys 180	Ser	Ile	туг	Ser	Gly 185		Va	1 T	hr	Gly	His 190	Glm	. M∈	35		
Ala																			
(2)	INF	ORMA	TION	FOR	SEQ	ID	NO:	197:										-	
		(	A) L B) T C) S D) T	ENGT YPE: TRAN OPOL	HARA H: 5 nuc DEDN	79 b leic ESS: lin	ase aci sir ear	pair .d	rs										
					YPE:		IA												
					:AL:														
	(iii	.) A1	TI-S	ENSE	E: NO	)													
	(i)			EMAN.	/KEY														
	(i:			NAME	/KEY TION				le										
	(x	i) S	EQUE	NCE	DESC	RIPT	'ION :	SEC	מו מ	NO:	: 19	7:							
AC Th	T TG r Cy 1	c GG s Gl	C TT y Ph	T GC le Al	C GA a As 5	C CT	C AT	rg go	Ly T	AC / yr : 10	ATC Ile	Pro	G CI	C GI	al G	GC ly 15 ·	Ala		48
CC Pr	C GT	G GG	y Gl	C GT .y Va	C GC	C AC	GA GO	la L	TG G eu G 25	AA ( lu )	CAT His	GG'	r GT y Va	al A	GG G rg A 30	CT la	GTG Val		96
GI GI	G GA	sp Gl	GC AT Ly II	C AF	AT TA	AT GO Yr Al	la T	CA-G hr G 40	GG A	AT .sn	CTC Leu	CC Pr	o G	ЭТ Т 1у С 45	GC I	cT	TTC Phe		144

TCT ATC TAC CTC TTG GCA CTT CTC TCG TGC CTG ACT GTT CCC ACC TCG

PCT/EP94/01323

Ser	Ile 50	Tyr	Leu	Leu	Ala	Leu 55	Leu	Ser	Cys	Leu	Thr 60	Val	Pro	Thr	Ser		
					AAT Asn 70												240
					ATA Ile												288
					CCC Pro												336
					CCC Pro											-	384
					AGA Arg												432
					TAT Tyr 150												480
					TCT Ser					Arg							528
					ATC Ile										ATG Met		576
GCA Ala																	579

#### (2) INFORMATION FOR SEQ ID NO: 198:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 193 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 198:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala 1 5 10 15

Pro Val Gly Gly Val Ala Arg Ala Leu Glu His Gly Val Arg Ala Val 20 \$25\$

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe

35 40 49

Ser Ile Tyr Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Thr Ser 50 55

Ala Ile His Tyr Arg Asn Ala Ser Gly Val Tyr His Val Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp His His Ile Leu His
85 90 95

Leu Pro Gly Cys Leu Pro Cys Val Arg Val Gly Asn Gln Ser Arg Cys
100 105 110

Trp Val Ala Leu Ser Pro Thr Val Ala Ala Pro Tyr Ile Gly Ala Pro 115 120 125

Val Glu Ser Phe Arg Arg His Val Asp Met Met Val Gly Ala Ala Thr 130 140

Val Cys Ser Ala Leu Tyr Ile Gly Asp Leu Cys Gly Gly Val Phe Leu 145 150 155 160

Val Gly Gln Met Phe Ser Phe Arg Pro Arg Arg His Trp Thr Thr Gln 165 170 175

Asp Cys Asn Cys Ser Ile Tyr Ala Gly His Ile Thr Gly His Gly Met 180 185 190

Ala

- (2) INFORMATION FOR SEQ ID NO: 199:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 1470 base pairs
    - (B) TYPE: nucleic acid(C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: NO
  - (ix) FEATURE:
    - (A) NAME/KEY: CDS
    - (B) LOCATION: 2..1470
  - (ix) FEATURE:
    - (A) NAME/KEY: mat_peptide
    - (B) LOCATION: 2..1467
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 199:

A T	CA C er P 1	CA CO	CG G.	AG C	TT C eu L 5	TA TO	CA C. er H.	AT AG	hr P	CA C TO L	TT A	CG G hr A	CA A	er Se	CC er LS		46
TTG Leu	CTG Leu	ATG Met	GAG Glu	GGT Gly 20	GTT Val	CAG Gln	GCG Ala	GCG Ala	CGC Arg 25	ATG Met	ACG Thr	TGA	TCA Ser	TAT Tyr 30	GCG Ala		94
ACG Thr	AGT Ser	GCC Ala	ATT Ile 35	CCC	AGG Arg	ACG Thr	CCA Pro	CCA Pro 40	CCA Pro	TTC Phe	TTG Leu	GGA Gly	TAG * 45	GCA Ala	CTG Leu		142
TCC Ser	TTG Leu	ACC Thr 50	AGG Arg	CAG Gln	AGA Arg	yra C@@	CTG Leu 55	GAG Glu	CTA Leu	GGC Gly	TCG Ser	TCG Ser 60	TCT Ser	TCG	CCA Pro		190
CGG Arg	CCA Pro 65	CCC Pro	CTC Leu	CCG Pro	GCA Ala	GTG Val 70	TGA *	CAA Gln	CGC Arg	Pro	ACC Thr 75	CCA Pro	ACA Thr	TCG Ser	AGG Arg	-	238
AAG Lys 80	TGG Trp	Pro	TGC Cys	CTC Leu	AGG Arg 85	AGG Arg	GGG Gly	AGG Arg	TTC Phe	Pro 90	TCT Ser	ACG Thr	GCA Ala	GAG Glu	CCA Pro 95		286
TTC Phe	CCC Pro	TTG Leu	CTT Leu	TTA Leu 100	TAA +	AGG Arg	GTG Val	GTA Val	GGC Gly 105	ATC Ile	TCA Ser	TCT Ser	TCT Ser	GCC Ala 110	ATT Ile		334
CCA Pro	AGA Arg	AAA Lys	AAT Asn 115	GTG Val	ATG Met	AAC Asn	TCG Ser	CCA Pro 120	AGC Ser	AAC Asn	TGA *	CCA Pro	GCC Ala 125	TGG Trp	GCG Ala		382
TGA *	ACG Thr	CCG Pro 130	TGG Trp	CAT His	ATT Ile	ATA Ile	GAG Glu 135	GTC Val	TAG *	ACG Thr	TCG Ser	CCG Pro 140	TCA Ser	TAC Tyr	CCA Pro		430
CAA Gln	CAG Gln 145	GAG Glu	ACG Thr	TGG Trp	TCG Ser	TGT Cys 150	GCA Ala	GCA Ala	CCG Pro	ACG Thr	CGC Arg 155	TCA Ser	TGA *	CGG Arg	GAT Asp		478
TCA Ser 160	CCG Pro	GCG Ala	ACT Thr	TTG Leu	ATT Ile 165	CTG Leu	TCA Ser	TAG *	ACT Thr	GCA Ala 170	ACT Thr	CCG Pro	CCG Pro	TCA Ser	CTC Leu 175		526
AGA Arg	CGG Arg	TGG Trp	ACT Thr	TCA Ser 180	GTC Val	TGG Trp	ATC Ile	CCA Pro	CTT Leu 185	TTA Leu	CCA Pro	TTG Leu	AGA Arg	CTA Leu 190	CCA Pro		574
CAG Gln	TGC <b>Cy</b> s	CCC Pro	AGG Arg 195	ACG Thr	CAG Gln	TGT Cys	CCA Pro	GAA Glu 200	GCC Ala	AGC Ser	GTT Val	GGG Gly	GCC Ala 205	GCA Ala	CGG Arg		622
GGA Gly	GAG Glu	GTA Val 210	GGC Gly	ACG Thr	GCA Ala	TAT Tyr	ACC Thr 215	GGT Gly	ATG Met	TCT Ser	CGG Arg	CTG Leu 220	GAG Glu	AGA Arg	GAC Asp		670
CGT Arg	CTG Leu	GCA Ala	TGT Cys	TCG Ser	ACT Thr	CCG Pro	TGG Trp	TGC Cys	TCT Ser	GTG Val	AGT Ser	GCT Ala	ACG Thr	ATG Met	CCG Pro		718

225			230			235			
	GGT Gly							Gly	766
	AAA Lys								814
	GGG Gly 275								862
	GAC Asp								910
	AAC Asn								958
	GTG Val								1006
	CTC Leu								1054
	CCC Pro 355								1102
	ATT Ile								1150
	GCC Ala								1198
	CTC Leu								1246
	CAA Gln								1294
	GAA Glu 435								1342
	ATC Ile			Gln			Leu		1390

GCA Ala	GCC Ala 465	ACG Thr	TCT Ser	GTG Val	TGG Trp	AAC Asn 470	AAG Lys	GCT Ala	GAG Glu	CAG Gln	TTC Phe 475	TGG Trp	CCA Pro	CAT His	ACA Thr	1438
			TCA Ser													1470

# (2) INFORMATION FOR SEQ ID NO: 197:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 1485 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA

### (1x) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 1..1485

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 197:

GCTGATGGAG	GGTGTTCAGG	CGGCGCGCAT	GACGTGATCA	#3#CCC3CC3	cmccca mmcc	120
		1000000001	dreditori Cr	IAIGCGACGA	GiGCCMiicc	140
CAGGACGCCA	CCACCATTCT	TGGGATAGGC	ACTGTCCTTG	ACCAGGCAGA	GACGGCTGGA	180
GCTAGGCTCG	TCGTCTTGGC	CACGGCCACC	CCTCCCGGCA	GTGTGACAAC	GCCCCACCCC	240
AACATCGAGG	AAGTGGCCCT	GCCTCAGGAG	GGGGAGGTTC	CCTTCTACGG	CAGAGCCATT	300
CCCCTTGCTT	TTATAAAGGG	TGGTAGGCAT	CTCATCTTCT	GCCATTCCAA	GAAAAATGT	360
GATGAACTCG	CCAAGCAACT	GACCAGCCTG	GGCGTGAACG	CCGTGGCATA	TTATAGAGGT	420
CTAGACGTCG	CCGTCATACC	CACAACAGGA	GACGTGGTCG	TGTGCAGCAC	CGACGCGCTC	480
ATGACGGGAT	TCACCGGCGA	CTTTGATTCT	GTCATAGACT	GCAACTCCGC	CGTCACTCAG	540
ACGGTGGACT	TCAGTCTGGA	TCCCACTTTT	ACCATTGAGA	CTACCACAGT	GCCCCAGGAC	600
GCAGTGTCCA	GAAGCCAGCG	TTGGGGCCGC	ACGGGGAGAG	GTAGGCACGG	CATATACCGG	<b>6</b> 60
TATGTCTCGG	CTGGAGAGAG	ACCGTCTGGC	ATGTTCGACT	CCGTGGTGCT	CTGTGAGTGC	720
TACGATGCCG	GATGTGCATG	GTACGATCTG	ACTCCTGCCG	AGACTACCGT	GAGGTTGCGC	780
GCTTACNTAA	ACACCCCCGG	GCTCCCTGTC	TGTCAGGACC	ATTTGGAATT	CTGGGAGGGG .	840
GTGTTCACGG	GGCTCACTAA	CATCGACGCT	CACATGCTGT	CACAGACCAA	ACAGGGTGGG	900
GAGAATTTCC	CATACCTTGT	AGCGTACCAA	GCAACAGTCT	GTGTTCGCGC	GAAAGCGCCC	960

TGTGCCAGGA CCATCACCAC CGGAGCTTCT ATCACATACT CCACTTACGG CAAGTTCCTT 60

CCCCCCAGCT	GGGACACAAT	GTGGAAATGC	ATGCTCCGTC	TCAAACCGAC	NTTAACTGGC	1020
CCTACTCCCC	TCTTGTACAG	GCTGGGGCCC	GTCCAGAATG	AGATCACACT	GACGCACCCC	1080
ATCACCAAGT	ACATTATGGC	TTGCATGTCT	GCGGACTTGG	AGGTCATTAC	CAGCACTTGG	1140
GTTCTGGTGG	GGGGCGTTGT	GGCGGCCCTG	GCGGCCTACT	GCTTGACGGT	GGGTTCGGTA	1200
GCCATAGTCG	GTAGGATCAT	CCTCTCTGGG	AAACCTGCCA	TCATTCCCGA	TAGGGAGGTA	1260
TTATACCAGC	AATTTGATGA	GATGGAGGAG	TGCTCGGCCT	CGTTGCCCTA	TATGGACGAA	1320
ACACGTGCCA	TTGCCGGACA	ATTCAAAGAG	AAAGTGCTCG	GCTTCATCAG	CACGACCGGC	1380
CAGAAGGCTG	AAACTCTGAA	GCCGGCAGCC	ACGTCTGTGT	GGAACAAGGC	TGAGCAGTTC	1440
TGGNCCACAT	ACATGTGGAA	CTTCATCAGT	GGGATACAAT	AATAG		_1485

- (2) INFORMATION FOR SEQ ID NO: 198:
  - (i) SEQUENCE CHARACTERISTICS.
    - (A) LENGTH: 484 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 198:
  - Cys Ala Arg Thr Ile Thr Thr Gly Ala Ser Ile Thr Tyr Ser Thr Tyr 1 5 10 15
  - Gly Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala His Asp Val 20 25 30
  - Ile Ile Cys Asp Glu Cys His Ser Gln Asp Ala Thr Thr Ile Leu Gly 35 40 45
  - Ile Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val 50 55 60
  - Val Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Thr Pro His Pro 65 70 75 80
  - Asn Ile Glu Glu Val Ala Leu Pro Gln Glu Gly Glu Val Pro Phe Tyr 85 90 95
  - Gly Arg Ala Ile Pro Leu Ala Phe Ile Lys Gly Gly Arg His Leu Ile 100 105 110
  - Phe Cys His Ser Lys Lys Lys Cys Asp Glu Leu Ala Lys Gln Leu Thr 115 120 125
  - Ser Leu Gly Val Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ala 130 140

Val 145	Ile	Pro	Thr	Thr	Gly 150	qzA	Val	Val	Val	<b>C</b> ys 155	Ser	Thr	Asp	Ala	Leu 160
Met	Thr	Gly	Phe	Thr 165	Gly	Asp	Phe	Asp	Ser 170	Val	Ile	Asp	Cys	Asn 175	Ser
Ala	Val	Thr	Gln 180	Thr	Val	Asp	Phe	Ser 185	Leu	Asp	Pro	Thr	Phe 190	Thr	lle
Glu	Thr	Thr 195	Thr	Val	Pro	Gln	Asp 200	Ala	Val	Ser	Arg	Ser 205	Gln	Arg	Trp
Gly	Arg 210	Thr	Gly	Arg	Gly	Arg 215	His	Gly	Ile	Tyr	Arg 220	Tyr	Val	Ser	Ala
Gly 225	Glu	Arg	Pro	Ser	Gly 230	Met	Phe	Asp	Ser	Val 235	Val	Leu	Cys	Glu	Cys 249
Tyr	Asp	Ala	Gly	Cys 245	Ala	Trp	Tyr	Asp	Leu 250	Thr	Pro	Ala	Glu	Thr 255	Thr
Val	Arg	Leu	Arg 260	Ala	Tyr	Xaa	Asn	Thr 265	Pro	Gly	Leu	Pro	Val 270	Cys	Gln
Asp	His	Leu 275	Glu	Phe	Trp	Glu	Gly 280	Val	Phe	Thr	Gly	Leu 285	Thr	Asn	Ile
Asp	Ala 290	His	Met	Leu	Ser	Gln 295	Thr	Lys	Gln	Gly	Gly 300	Glu	Asn	Phe	Pro
Tyr 305	Leu	Val	Ala	Tyr	Gln 310	Ala	Thr	Val	Cys	Val 315	Arg	Ala	Lys	Ala	Pro 320
Pro	Pro	Ser	Ττ⊃	Asp 325		Met	Trp	Lys	Cys 330		Leu	Arg	Leu	1335	
Xaa	Leu	Thr	Gly 340	Pro	Thr	Pro	Leu	Leu 345	-	Arg	Leu	Gly	9ro 350		Gln
Asn	Glu	Ile 355		Leu	Thr	His	Pro 360		Thr	Lys	Tyr	1le 365		. Ala	Cys
Met	Ser 370		. Asp	Leu	. Glu	. Val		Thr	Ser	Thr	380		Leu	ı Val	. Gly
Gly 385	Val	Val	Ala	Ala	1 Leu 390		Ala	Туг	Cys	399		Val	. Gly	/ Se:	400
Ala	Ile	Val	. Gly	Arg 405		: Ile	e Leu	Ser	Gly 410	_	Pro	Ala	a Ile	11:	e Pro
Asp	Arg	Glu	420		ı Tyr	Gli	ı Gln	1 Phe 429		o Gla	ı Met	: Glu	430		s Ser
Ala	Ser	Le: 433		туг	. Met	As	9 Glu 440	-	r Arg	g Ala	a Ile	e Ala 44		y Gl	n Phe

Lys Glu Lys Val Leu Gly Phe Ile Ser Thr Thr Gly Gln Lys Ala Glu 450 455 460

Thr Leu Lys Pro Ala Ala Thr Ser Val Trp Asn Lys Ala Glu Gln Phe 465 470 475 480

Trp Xaa Thr Tyr

- (2) INFORMATION FOR SEQ ID NO: 199:
  - (1) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 1485 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA
  - (1x) FEATURE:
    - (A) NAME/KEY: CDS
    - (B) LOCATION: 1..1485
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 199:

TGTGCCAGGA	CCATCACCAC	CGGAGCTTCT	ATCACATACT	CCACTTACGG	CAAGTTCCTT	60
GCTGATGGAG	GGTGTTCAGG	CGGCGCGTAT	GACGTGATCA	TATGCGACGA	GTGCCATTCC	120
CAGGACGCCA	CCACCATTCT	TGGGATAGGC	ACTGTCCTTG	ACCAGGCAGA	GACGGCTGGA	180
GCTAGGCTCG	TCGTCTTGGC	CACGGCCACC	CCTCCCGGCA	GTGTGACAAC	GCCCCACCCC	240
AACATCGAGG	AAGTGGCCCT	GCCTCAGGAG	GGGGAGGTTC	CCTTCTACGG	CAGAGCCATT	300
CCCCTTGCTT	TTATAAAGGG	TGGTAGGCAT	CTCATCTTCT	GCCATTCCAA	GAAAAAATGT	360
GATGAACTCG	CCAAGCAACT	GACCAGCCTG	GGCGTGAACG	CCGTGGCATA	TTATAGAGGT	420
CTAGACGTCG	CCGTCATCCC	CACAGCAGGA	GACGTGGTCG	TGTGCAGCAC	CGACGCGCTC	480
ATGACGGGAT	TCACCGGCGA	CTTTGATTCT	GTCATAGACT	GCAACTCCGC	CGTCACTCAG	540
ACGGTGGACT	TCAGTCTGGA	TCCCACTTTT	ACCATTGAGA	CTACCACAGT	GCCCCAGGAC	600
GCAGTGTCCA	GAAGCCAGCG	TAGGGGCCGC	ACGGGGAGAG	GTAGGCACGG	CATATACCGG	660
TATGTCTCGG	CTGGAGAGAG	ACCNTCTGAC	ATGTTCGACT	CCGTGGTGCT	CTGTGAGTGC	720
TACGATGCCG	GATGTGCGTG	GTATGATCTG	ACTCCTGCCG	AGACTACCGT	GAGGTTGCGC	780
GCTTACATAA	ACACCCCCGG	GCTCCCTGTC	TGTCAGGACC	ATTTGGAATT	CTGGGAGGGG	840
GTGTTCACGG	GGCTCACTAA	CATCGACGCT	CACATGCTGT	CACAGACCAA	ACAGGGTGGG	900
GAGAATTTNC	CATACCTTGT	AGCGTACCAA	GCAACAGTCT	GTGTTCGCGC	GAAAGCGCCC	960

CCCCCAGCT	GGGACACAAT	GTGGAAATGC	ATGCTCCGTC	TCAAACCGAC	TTTAACTGGC	1020
CCTACTCCCC	TCTTGTACAG	GCTGGGGCCC	GTCCAGANTG	AGATCACACT	GACGCACCCC	1080
ATCACCAAGT	ACATTATGGC	TTGCATGTCT	GCGGACTTGG	AGGTCATTAC	CANCACTTGG	1140
GTTCTGGTGG	GGGGCGTTGT	GGCGGCCCTG	GCGGCCTACT	GCTTGACGGT	GGGTTCGGTA	1200
GCCATAGTCG	GTAGGATCAT	CCTCTCTGGG	AAACCTGCCA	TCATTCCCGA	TAGGGAGGCA	1260
TTATACCAGC	AATTTGATGA	GATGGAGGAG	TGCTCGGCCT	CGTTGCCCTA	TATGGACGAG	1320
ACACGTGCCA	TTGCCGGACA	ATTCAAAGAG	AAAGTGCTCG	GCTTCATCAG	CACGACCGGC	1380
CAGAAGGCTG	AAACTCTGAA	GCCGGCAGCC	ACGTCTGTGT	GGAACAAGGC	TGAGCAGTTC	1440
TGGGCCACAT	ACATGTGGAA	CTTCATCAGC	GGGATACAAT	AATAG		1485

# (2) INFORMATION FOR SEQ ID NO: 200:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 484 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 200:
- Cys Ala Arg Thr Ile Thr Thr Gly Ala Ser Ile Thr Tyr Ser Thr Tyr
- Gly Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Val
- Ile Ile Cys Asp Glu Cys His Ser Gln Asp Ala Thr Thr Ile Leu Gly 40
- Ile Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val 55
- Val Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Thr Pro. His Pro
- Asn Ile Glu Glu Val Ala Leu Pro Gln Glu Gly Glu Val Pro Phe Tyr
- Gly Arg Ala Ile Pro Leu Ala Phe Ile Lys Gly Gly Arg His Leu Ile 105
- Phe Cys His Ser Lys Lys Lys Cys Asp Glu Leu Ala Lys Gln Leu Thr 120

Ser	Leu 130	Gly	Val	Asn	Ala	Val 135	Ala	Tyr	Tyr	Arg	Gly 140	Leu	ązA	Val	Ala
Val 145	Ile	Pro	Thr	Ala	Gly 150	Asp	Val	Val	Val	Cys 155	Ser	Thr	qzA	Ala	Leu 160
Met	Thr	Gly	Phe	Thr 165	Gly	Asp	Phe	Asp	Ser 170	Val	Ile	ąsA	Cys	Asn 175	Ser
Ala	Val	Thr	Gln 180	Thr	Val	Asp	Phe	Ser 185	Leu	Asp	Pro	Thr	Phe 190	Thr	Ile
Glu	Thr	Thr 195	Thr	Val	Pro	Gln	Asp 200	Ala	Val	Ser	Arg	Ser 205	Gln	Arg	Arg
Gly	Arg 210	Thr	Gly	Arg	Gly	Arg 215	His	Gly	Ile	Tyr	Arg 220	Tyr	Val	Ser	Ala -
Gly 225	Glu	Arg	Xaa	Ser	Asp 230	Met	Phe	Asp	Ser	Val 235	Val	Leu	Cys	Glu	Cys 240
Tyr	Asp	Ala	Gly	Cys 245	Ala	Irb	Tyr	Asp	Leu 250	Thr	Pro	Ala	Glu	Thr 255	Thr
Val	Arg	Leu	Arg 260	Ala	īÀī	Ile	Asn	Thr 265	Pro	Gly	Leu	Pro	Val 270	Cys	Gln
Asp	His	Leu 275	Glu	Phe	Trp	Glu	Gly 280	Val	Phe	Thr	Gly	Leu 285	Thr	Asn	Ile
Asp	Ala 290	His	Met	Leu	Ser	Gln 295	Thr	Lys	Gln	Gly	Gly 300	Glu	Asn	Xaa	Pro
Tyr 305	Leu	Val	Ala	Tyr	Gln 310	Ala	Thr	Val	Cys	Val 315	Arg	Ala	Lys	Ala	Pro 320
Pro	Pro	Ser	Trp	Asp 325	Thr	Met	Trp	Lys	Cys 330	Met	Leu	Arg	Leu	Lys 335	Pro
Thr	Leu	Thr	Gly 340	Pro	Thr	Pro	Leu	Leu 345	Tyr	Arg	Leu	Gly	Pro 350	Val	Gln
Xaa	Glu	Ile 355	Thr	Leu	Thr	His	Pro 360	Ile	Thr	Lys	Tyr	Ile 365	Met	Ala	Cys
Met	Ser 370	Ala	Asp	Leu	Glu	Val 375	Ile	Thr	Xaa	Thr	Trp 380	Val	Leu	Val	Gly
385		Val			390					395					400
Ala	Ile	Val	Gly	Arg 405	Ile	Ile	Leu	Ser	Gly 410	Lys	Pro	Ala	Ile	Ile 415	Pro
Asp	Arg	Glu	Ala 420	Leu	Tyr	Gln	Gln	Phe 425	Asp	Glu	Met	Glu	Glu 430	Cys	Ser
Ala	Ser	Leu	Pro	Tyr	Met	qzA	Glu	Thr	Arg	Ala	Ile	Ala	Gly	Gln	Phe

286

258

435 440 445 Lys Glu Lys Val Leu Gly Phe Ile Ser Thr Thr Gly Gln Lys Ala Glu 455 Thr Leu Lys Pro Ala Ala Thr Ser Val Trp Asn Lys Ala Glu Gln Phe 475 Trp Ala Thr Tyr (2) INFORMATION FOR SEQ ID NO: 201: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 340 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: cDNA (iii) HYPOTHETICAL: NO (iii) ANTI-SENSE: NO (ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 2..340 (1x) FEATURE: (A) NAME/KEY: mat peptide (B) LOCATION: 2..337 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 201: C TCC ACT GTG ACT GAG AGA GAC ATC AGG GTC GAA GAA GAA GTC TAT 46 Ser Thr Val Thr Glu Arg Asp Ile Arg Val Glu Glu Val Tyr CAG TGT TGT GAT CTG GAG CCC GAG GCC CGC AAG GTA ATA ACC GCC CTC 94 Gln Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Thr Ala Leu ACG GAG AGA CTC TAC GTG GGC GGC CCT ATG TAC AAT AGC AAG GGA GAC 142 Thr Glu Arg Leu Tyr Val Gly Gly Pro Met Tyr Asn Ser Lys Gly Asp CTT TGC GGG TAT CGC AGG TGC CGC GCA AGC GGC GTA TAT ACC ACC AGC 190 Leu Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser

GCT GCG GGG CTG AAG GAC TGC ACC ATG CTG GTT TGC GGT GAC GAC TTA

TTC GGG AAC ACA CTG ACG TGC TAC CTT AAA GCC TCA GCA GCC ATC AGG

Phe Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Ile Arg

70

5.0

GTC GTG ATC GCT GAA AGC GGT GGC GTC GAG GAG GAC AAG CGA GCC CTC

Val Val Ile Ala Glu Ser Gly Gly Val Glu Glu Asp Lys Arg Ala Leu

100 105 110

GGA GCT Gly Ala 340

- (2) INFORMATION FOR SEQ ID NO: 202:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 113 amino acids
    - (B) TYPE: amino acid
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 202:

Ser Thr Val Thr Glu Arg Asp Ile Arg Val Glu Glu Glu Val Tyr Gln

1 5 10 15

Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Thr Ala Leu Thr

20 25 30

Glu Arg Leu Tyr Val Gly Gly Pro Met Tyr Asn Ser Lys Gly Asp Leu 35 40 45

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Phe 50 55 60

Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Ile Arg Ala 65 70 75 80

Ala Gly Leu Lys Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Val Ile Ala Glu Ser Gly Gly Val Glu Glu Asp Lys Arg Ala Leu Gly
100 105 110

Ala

- (2) INFORMATION FOR SEQ ID NO: 203:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 340 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (11) MOLECULE TYPE: cDNA
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: NO

260

	(ix)	-	AN (.	ME/K	EY:		40									
	(ix)		.) NA	ME/K	EY:	_		ide								
	(xi)	SEC	UENC	E DE	SCRI	PTIC	N: S	EQ I	סא פ	: 20	3:					
		A GT ir Va							g Va					i Ty		46
CAG	TGT	TGT	GAC	CTG	GAG	CCT	GAA	ACC	CGC	AAG	GTA	ATA	TCT	GCC	CTC	94
Gln	Cys	Cys	Asp	Leu 20	Glu	Pro	Glu	Thr	Arg 25	Lys	Val	Ile	Ser	Ala 30	Leu	-
ACT	GAA	AGA	CTC	TAT	GTG	GGC	GGT	CCC	ATG	CAC	AAC	AGC	AGG	GGA	GAC	142
Thr	Glu	Arg	Leu 35	Tyr	Val	Gly	Gly	Pro 40	Met	His	Asn	Ser	Arg 45	Gly	ązk	
CTA	TGC	GGG	TAC	CGT	AGA	TGC	CGC	GCG	AGC	GGC	GTA	TAC	ACC	ACA	AGC	190
Leu	Cys	Gly 50	Tyr	Arg	Arg	Cys	Arg 55	Ala	Ser	Gly	Val	Tyr 60	Thr	Thr	Ser	
TTC	GGG	AAC	ACT	CTG	ACG	TGC	TTC	CTC	AAG	GCC	ACA	GCG	GCC	ACC	AAA	238
Phe	Gly 65	Asn	Thr	Leu	Thr	Cys 70	Phe	Leu	Lys	Ala	Thr 75	Ala	Ala	Thr	Lys	
GCC	GCT	GGC	СТА	AAG	GAC	TGC	ACC	ATG	TTG	GTG	TGT	GGT	GAC	GAC	TTA	286
Ala	Ala	Gly	Leu	Lys	qzA	Cys	Thr	Met	Leu	Val	Cys	Gly	Asp	qaA	Leu	
80					85					90					95	
GTC	GTT	ATC	GCC	GAA	AGC	GAT	GGT	GTC	GAA	GAG	GAC	CGC	CGA	GCC	CTC	334
Val	Val	Ile	Ala	Glu	Ser	Asp	Gly	Val	Glu	Glu	Asp	Arg	Arg	Ala	Leu	
				100					105					110		

(2) INFORMATION FOR SEQ ID NO: 204:

GGA GCT Gly Ala

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 113 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 204:

Ser Thr Val Thr Glu Arg Asp Ile Arg Val Glu Glu Glu Val Tyr Gln 1 5 10 15

Cys	Cys	Asp	Leu 20	Glu	Pro	Glu	Thr	Arg 25	Lys	Val	Ile	Ser	Ala 30	Leu	Thr		
Glu	Arg	Leu 35	Tyr	Val	Gly	Gly	Pro 40	Met	His	Asn	Ser	Arg 45	Gly	Asp	Leu		
Cys	Gly 50	Tyr	Arg	Arg	Cys	A <b>r</b> g 55	Ala	Ser	Gly	Val	TY= 60	Thr	Thr	Ser	Phe		
Gly 65	Asn	Thr	Leu	Thr	Cys 70	Phe	Leu	Lys	Ala	Thr 75	Ala	Ala	Thr	Lys	Ala 80		
Ala	Gly	Leu	Lys	Asp 85	Cys	Thr	Met	Leu	Val 90	Суз	Gly	Asp	Asp	Leu 95	Val		
Val	Ile	Ala	Glu 100	Ser	Asp	Gly	Val	Glu 105	Glu	Asp	Arg	Arg	Ala 110	Leu	Gly	-	
Ala																	
(2)	INF	ORMA	TION	FOR	SEQ	ID 1	NO:	205:									
	13	) GE	QUEN	רב ר.	יבקבי	מבתר	7577	cs ·									
	\-	(.	A) L	ENGT	H: 3	40 b	ase	pair	s					•			
			B) T C) S														
			D) T					915									
	(ii	) MO	LECU	LE T	YPE:	CDN	Α										
	(ıii	) HY	POTH	ETIC	AL:	NO									,	•	
	(ıii	MA (	TI-S	ENSE	: NO												
	(ix	) FE	ATUR	E :													
	•	(	A) N	AME/													
		(	B) L	OCAT	: NOI	2	340										
	(ix	) FE	ATUR	Ξ:													
			(A) N (B) L						2								
	(xi		EQUEN						ID 1	NO: 2	205:						
C 1	raa A	ica (	STG A	וכר פ	AA A	AGG C	at A	ATC A	AGG J	ACC (	GAG (	GAA (	GAG 2	ATC '	TÁC		46
			/al T														
CAG	TG	TG	GAC	CTO	GAC	G CC	GA)	A GC	C CG	CAAC	G GT	G AT	A TC	c gc	C CTA		94
					ı Glu					g Ly:				r Al	a Leu O		
AC	G GAJ	A AG	A CTO	TAC	GTC	G GG	c GG	T CC	C AT	G TA	C AA	c TC	C AA	G GG	G GAC	1	42
Th	Gli	ı Ar	-		va!	1 G1	y Gl	y Pr 4		t Ty	r As	n Se		s Gl 5	gzA y.		
			3 9	2				4	J				4	,			

CTA Leu	TGC Cys	GGG Gly 50	CAA Gln	CGG Arg	AGG Arg	TGC Cys	CGC Arg 55	GCA Ala	AGC Ser	GGG Gly	GTC Val	TAC Tyr 60	ACC Thr	ACC Thr	AGC Ser	190
TTC Phe	GGG Gly 65	AAC Asn	ACT Thr	GTA Val	ACG Thr	TGT Cys 70	TAT Tyr	CTC Leu	AAG Lys	GCC Ala	GIT Val 75	GCG Ala	GCT Ala	ACT Thr	AGG Arg	238
GCC Ala 80	GCA Ala	GGT Gly	CTG Leu	AAA Lys	GGT Gly 85	TGC Cys	AGC Ser	ATG Met	CTG Leu	GTT Val 90	TGT Cys	GGA Gly	GAC Asp	GAC Asp	TTA Leu 95	286
GTC Val	GTC Val	ATC Ile	TGC Cys	GAG Glu 100	AGC Ser	GGC Gly	GGC Gly	GTA Val	GAG Glu 105	GAG Glu	GAT Asp	GCA Ala	AGA Arg	GCC Ala 110	CTC Leu	334
CGA Arg	GCC Ala															- 340

# (2) INFORMATION FOR SEQ ID NO: 206:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 113 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 206:

Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Glu Ile Tyr Gln
1 5 10 15

Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Ser Ala Leu Thr 20 25 30

Glu Arg Leu Tyr Val Gly Gly Pro Met Tyr Asn Ser Lys Gly Asp Leu
35 40 45

Cys Gly Gln Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Phe 50 60

Gly Asn Thr Val Thr Cys Tyr Leu Lys Ala Val Ala Ala Thr Arg Ala 65 70 75 80

Ala Gly Leu Lys Gly Cys Ser Met Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Val Ile Cys Glu Ser Gly Gly Val Glu Glu Asp Ala Arg Ala Leu Arg 100 105 110

Ala

(2) INFORMATION FOR SEQ ID NO: 207:

(1) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 340 base pairs

(B) TYPE: nucleic acid	
(C) STRANDEDNESS: single	
(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: cDNA	
(iii) HYPOTHETICAL: NO	
(iii) ANTI-SENSE: NO	
(ix) FEATURE:	
(A) NAME/KEY: CDS (B) LOCATION: 2340	
(in) Frame	
<pre>(ix) FEATURE:     (A) NAME/KEY: mat_peptide</pre>	-
(B) LOCATION: 2337	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 207:	
C TCC ACG GTG ACT GAA AGG GAC ATT AGG GTC GAG GAA GAG ATC TAC Ser Thr Val Thr Glu Arg Asp Ile Arg Val Glu Glu Ile Tyr 1 5 10 15	46
CAG TGC TGT GAC CTG GAG CCC GAG GCA CGC AAG GTG ATA TCC GCT CTC	94
Gln Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Ser Ala Leu 20 25 30	
ACA GAA AGA CTC TAC AAG GGC GGC CCC ATG TAT AAC AGC AAG GGG GAC Thr Glu Arg Leu Tyr Lys Gly Gly Pro Met Tyr Asn Ser Lys Gly Asp	142
35 40 45	
CTA TGC GGG CTT CGG AGG TGC CGC GCA AGC GGG GTA TAC ACC ACA AGC	190
Leu Cys Gly Leu Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser 50 60	
TTC GGG AAC ACG GTG ACA TGC TAC CTT AAA GCC ACA GCA GCC ACC AGG	238
Phe Gly Asn Thr Val Thr Cys Tyr Leu Lys Ala Thr Ala Ala Thr Arg	230
65 70 75	
GCT GCA GGG CTG AAA GAT TGC ACT ATG CTG GTA TGC GGT GAC GAC TTA	286
Ala Ala Gly Leu Lys Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu 80 85 90 95	
GTC GTT ATT GCC GAA AGC GGT GGC GTG GAG GAC GCC CGA GCC CTC	334
Val Val Ile Ala Glu Ser Gly Gly Val Glu Glu Asp Ala Arg Ala Leu	
100 105 110	
CGA GCC	340
Arg Ala	

(2) INFORMATION FOR SEQ ID NO: 208:

(i) S	QUENCE CHARACTERISTICS:
(A	LENGTH: 113 amino acids
(B	TYPE: amino acid
(D	TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 208:

Ser Thr Val Thr Glu Arg Asp Ile Arg Val Glu Glu Glu Ile Tyr Gln

1 5 10 15

Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Ser Ala Leu Thr 20 25 30

Glu Arg Leu Tyr Lys Gly Gly Pro Met Tyr Asn Ser Lys Gly Asp Leu 35 40 45

Cys Gly Leu Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Pne 50 60

Gly Asn Thr Val Thr Cys Tyr Leu Lys Ala Thr Ala Ala Thr Arg Ala 65 70 75 80

Ala Gly Leu Lys Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Val Ile Ala Glu Ser Gly Gly Val Glu Glu Asp Ala Arg Ala Leu Arg
100 105 110

Ala

- (2) INFORMATION FOR SEQ ID NO: 209:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 340 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: NO
  - (ix) FEATURE:
    - (A) NAME/KEY: CDS
    - (B) LOCATION: 1..340
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 209:

CCCCACCGTG ACNGAGAGGG ACNTCAGGGT CGAGGAAGAG GTCTATCAGT GCTGTAATCT

GGAGNCCGAT GNCCGCAAGG TCATCAACGC CCTCACAGAG AGACTCTACG TGGGCGGCCC

TATGCACAAC	AGCAAGGGAG	ACCTGTGTGG	CATCCGTAGA	TGCCGCGCGA	GCGGCGTTTA	180
CACCACGAGC	TTCGGAAACA	CGCTGACTTG	CTACCTCAAA	GCCACAGCGG	CCACCAGGGC	240
CGCGGGCTTG	AAGGATTGCA	CCATGCTGGT	CTGCGGNGAC	GACCTGGTTG	TCATTGCTGA	300
GAGCATTGGC	ATAGACGAGG	ACAAGCAAGC	CCTCCGMACT			340

- (2) INFORMATION FOR SEQ ID NO: 210:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 113 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA
  - (iii) HYPOTHETICAL: NO
  - (111) ANTI-SENSE: NO
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 210:

Pro Thr Val Thr Glu Arg Asp Xaa Arg Val Glu Glu Glu Val Tyr Gln
1 5 10 15

Cys Cys Asn Leu Glu Xaa Asp Xaa Arg Lys Val Ile Asn Ala Leu Thr 20 25 30

Glu Arg Leu Tyr Val Gly Gly Pro Met His Asn Ser Lys Gly Asp Leu 35 40 45

Cys Gly Ile Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Phe 50 60

Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Thr Ala Ala Thr Arg Ala 65 70 75 80

Ala Gly Leu Lys Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Val Ile Ala Glu Ser Ile Gly Ile Asp Glu Asp Lys Gln Ala Leu Arg

Thr

- (2) INFORMATION FOR SEQ ID NO: 211:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 340 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA

- (iii) HYPOTHETICAL: NO
- (iii) ANTI-SENSE: NO
- (1x) FEATURE:
  - (A) NAME/KEY: CDS
  - (B) LOCATION: 1.:340
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 211:

CTCGACTGTG	NCCGAGAGGG	ACATCAGGAC	AGAGGGAGAG	GTCTATCAGT	GTTGCGACCT		60
GGAACCGGAA	GCCCGCAAGG	TAATCACCGC	CCTCACTGAG	AGACTCTATG	TGGGCGGACC		120
CATGTTCAAC	AGCAAGGGAG	ACCTGTGCGG	ACAACGCCGG	TGCCGCGCAA	GCGGCGTGTT	-	180
CACCACCAGC	TTCGGGAACA	CACTGACGTG	СТАССТТАЛА	GCCACAGCTG	CTACTAGAGC		240
AGCCGGCTTA	AAAGATTGCA	CCATGCTGGT	CTGCGGTGAC	GACTTAGTCG	TTATTTCCGA		300
GAGCGCCGGT	GTGGAGGAGG	ATCCCANAAC	CCNINCGACCN				340

- (2) INFORMATION FOR SEQ ID NO: 212:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 113 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: NO
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 212:

Ser Thr Val Xaa Glu Arg Asp Ile Arg Thr Glu Gly Glu Val Tyr Gln 1 5 10 15

Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Thr Ala Leu Thr 20 25 30

Glu Arg Leu Tyr Val Gly Gly Pro Met Phe Asn Ser Lys Gly Asp Leu 35 40 45

Cys Gly Gln Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser Phe 50 55

Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Thr Ala Ala Thr Arg Ala

	65					70					75					80	
	Ala	Gly	Leu	Lys	Asp 85	Cys	Thr	Met	Leu	Val 90	Cys	Gly	Asp	Asp	Leu 95	Val	
	Val	Ile	Ser	Glu 100	Ser	Ala	Gly	Val	Glu 105	Glu	Asp	Pro	Xaa	Thr	Xaa	Arg	
	Pro																
(2)	INFO	RMAT	ION :	FCR .	SEQ	ID N	O: 2	13:									
	(i)	(A (B (C	UENC: ) LE: ) TY: ) ST: ) TO	NGTH PE::: RAND	: 34 nucl EDNE	0 ba eic SS:	se p acid sing	airs								-	
	(ii)	MOL	ECUL	E TY	PE:	CDNA											
(	iii)	HYP	OTHE	TICA	L: N	o											
(	iii)	ANT	I-SE	NSE:	NO												
	(ix)	A)	TURE NA	ME/K			40										
	(ix)	(A	TURE ) NA ) LO	ME/K		_		ide									
	(xi)	SEC	UENC	E DE	SCRI	PTIC	N: S	EQ I	D NO	: 21	3:						
			C AC						g Va					e Ty			46
			GAC Asp														94
			CTT Leu 35														142
			TAT Tyr														190
			ACC Thr														238
GCT	GCG	AAG	CTC	CAG	GAC	TGC	ACG	ATG	CIC	GTG	TGC	GGG	GAC	GAC	CTT		286

200																	
Ala 80	Ala	Lys	Leu	Gln	Asp 85	Cys	Thr	Met	Leu	<b>V</b> al 90	Cys	Gly	Asp	Asp	Leu 95		
GTC Val	GTT Val	ATC Ile	TGT Cys	GAA Glu 100	AGC Ser	GCG Ala	GGA Gly	ACC Thr	CAA Gln 105	GAG Glu	GAC Asp	GCG Ala	GCG Ala	AGC Ser 110	CTA Leu	3	34
CGA Arg																3	40

- (2) INFORMATION FOR SEQ ID NO: 214:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 113 amino acids
    - (B) TYPE: amino acid
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 214:

Ser Thr Val Thr Glu Asn Asp Ile Arg Val Glu Glu Ser Ile Tyr Gln 1 5 10 15

Cys Cys Asp Leu Ala Pro Glu Ala Arg Gln Ala Ile Lys Ser Leu Thr
20 25 30

Glu Arg Leu Tyr Ile Gly Gly Pro Leu Thr Asn Ser Lys Gly Gln Asn 35 40 45

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Ser Cys
50 55 60

Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Cys Arg Ala 65 70 75 80

Ala Lys Leu Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu Arg 100 105 110

Val

- (2) INFORMATION FOR SEQ ID NO: 215:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 340 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA

- (	(iii	HYPOTHETICAL:	NO
٠,		nifolimitam.	TAC

(iii) ANTI-SENSE: NO

### (ix) FEATURE:

(A) NAME/KEY: CDS
(B) LOCATION: 2..340

## (ix) FEATURE:

(A) NAME/KEY: mat_peptide(B) LOCATION: 2..340

### (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 215:

			ACA GAA GAA TCC Thr Glu Glu Ser 10		46
CAA GCT TGT Gln Ala Cys	TCC CTG CCC C Ser Leu Pro C 20	Sln Glu Ala Ar	GA ACT GTC ATA C rg Thr Val Ile H 25	AC TCG CTC is Ser Leu 30	94
			CG ATA AAC AGC A et Ile Asn Ser L		142
			GC GGT GTT TTC A er Gly Val Phe T 60		190
			AA GCC CTT GCA G ys Ala Leu Ala A 75		238
			TG GTG TGT GGA G eu Val Cys Gly A 90		286
			AG GAG GAC GAG C Lu Glu Asp Glu A DS		334
AGA GCT Arg Ala					340

## (2) INFORMATION FOR SEQ ID NO: 216:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 113 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 216:

Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Ser Ile Tyr Gln
1 5 10 15

Ala Cys Ser Leu Pro Gln Glu Ala Arg Thr Val Ile His Ser Leu Thr
20 25 30

Glu Arg Leu Tyr Val Gly Gly Pro Met Ile Asn Ser Lys Gly Gln Ser 35 40 45

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser Met 50 55

Gly Asn Thr Met Thr Cys Tyr Ile Lys Ala Leu Ala Ala Cys Lys Ala 65 70 75 80

Ala Gly Ile Val Asp Pro Val Met Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Val Ile Ser Glu Ser Gln Gly Asn Glu Glu Asp Glu Arg Asn Leu Arg 100 105 110

Ala

- (2) INFORMATION FOR SEQ ID NO: 217:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 340 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: cDNA
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: NO
  - (ix) FEATURE:
    - (A) NAME/KEY: CDS
    - (B) LOCATION: 2..340
  - (ix) FEATURE:
    - (A) NAME/KEY: mat_peptide
    - (B) LOCATION: 2..340
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 217:
- C TCG ACT GTC ACT GAA CAG GAC ATC AGG GTG GAA GAG GAG ATA TAT

  Ser Thr Val Thr Glu Gln Asp Ile Arg Val Glu Glu Glu Ile Tyr

  1 5 10 15
- CAA TGC TGC AAC CTT GAA CCG GAG GCC AGG AAA GTG ATC TCC TCC CTC 94
  Gln Cys Cys Asn Leu Glu Pro Giu Ala Arg Lys Val Ile Ser Ser Leu

AGA GCC

Arg Ala

			20				25				30		
	GAG Glu												142
	TGT Cys												190
	GGC Gly 65												238
	GCA Ala												286
	GTG Val		Сľл	Asp	Gly	Val	ζεA	Glu	Arg	Ala		-	334

# (2) INFORMATION FOR SEQ ID NO: 213:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 113 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (11) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 218:

Ser Thr Val Thr Glu Gln Asp Ile Arg Val Glu Glu Glu Ile Tyr Gln
1 5 10 15

Cys Cys Asn Leu Glu Pro Glu Ala Arg Lys Val Ile Ser Ser Leu Thr 20 25 30

Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly Ala Gln
35 40 45

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr Ser Phe 50 60 .

Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Thr Ala Ala Lys Ala 65 70 75 80

Ala Gly Leu Arg Asn Pro Asp Phe Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Val Val Ala Glu Ser Asp Gly Val Asp Glu Asp Arg Ala Ala Leu Arg
100 105 110

Ala

- (2) INFORMATION FOR SEQ ID NO: 219:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 219:

Arg Ser Glu Gly Arg Thr Ser Trp Ala Gln
1 5 10

- (2) INFORMATION FOR SEQ ID NO: 220:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (11) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 220:

Arg Ser Glu Gly Arg Thr Ser Trp Ala Gln 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 221:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (11) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 221:

Arg Thr Glu Gly Arg Thr Ser Trp Ala Gln
1 5 10

- (2) INFORMATION FOR SEQ ID NO: 222:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 629 base pairs

- (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
- (iii) HYPOTHETICAL: NO

(ii) MOLECULE TYPE: cDNA

- (iii) ANTI-SENSE: NO
- (ix) FEATURE:

(A) NAME/KEY: CDS (B) LOCATION: 3..629

### (ix) FEATURE:

(A) NAME/KEY: mat_peptide (B) LOCATION: 3..629

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 222:

				CAC ATA G His Ile A	47
				TTC TCG Phe Ser	 95
 				GCT CCT Ala Pro 45	143
				AAG CCA Lys Pro 60	191
				GTC CAA Val Gln	239
 				GCA TGC Ala Cys	287
			Val Leu	CTT GGA	335
 	-			TGT GTT Cys Val	383
 		Lys Pro		GTT CCA Val Pro	

GAG Glu	GTG Val 145	TTG Leu	TAT Tyr	CAA Gln	CAA Gln	TAC Tyr 150	GAT Asp	GAG Glu	ATG Met	GAA Glu	GAG Glu 155	TGC Cys	TCA Ser	CAA Gln	GCT Ala	479
GCC Ala 160	CCA Pro	TAT Tyr	ATC Ile	GAA Glu	CAA Gln 165	GCT Ala	CAG Gln	GTA Val	ATA Ile	GCT Ala 170	CAC His	CAG Gln	TTC Phe	AAG Lys	GAA Glu 175	527
AAA Lys	GTC Val	CTT Leu	GGA Gly	TTG Leu 180	CTG Leu	CAG Gln	CGA Arg	GCC Ala	ACC Thr 185	CAA Gln	CAA Gln	CAA Gln	GCT Ala	GTC Val 190	ATT Ile	\$75
GAG Glu	CCC Pro	ATA Ile	GTA Val 195	ACT Thr	ACC Thr	AAC Asn	TGG Trp	CAA Gln 200	AAG Lys	CTT Leu	GAG Glu	GCC Ala	TTT Phe 205	TGG Trp	CAC His	623
AAG Lys																629

## (2) INFORMATION FOR SEQ ID NO: 223:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 209 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (11) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 223:

Asp Phe Trp Glu Ser Val Phe Thr Gly Leu Thr His Ile Asp Ala His 1 5 10 15

Phe Leu Ser Gln Thr Lys Gln Gln Gly Leu Asn Phe Ser Phe Leu Thr 20 25 30

Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro Ser
35 40 45

Trp Asp Glu Met Trp Lys Cys Leu Val Arg Leu Lys Pro Thr Leu His
50 55 60

Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Pro Val Gln Asn Glu Ile 65 70 75 80

Cys Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala Cys Met Ser Ala

Asp Leu Glu Val Thr Thr Ser Thr Trp Val Leu Leu Gly Gly Val Leu 100 105 110

Ala Ala Leu Ala Ala Tyr Cys Leu Ser Val Gly Cys Val Val Ile Val 115 120 125

Gly His Ile Glu Leu Gly Gly Lys Pro Ala Ile Val Pro Asp Lys Glu 130 135 140

Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala His Gln Phe Lys Glu Lys 165 170 175

Val Leu Gly Leu Leu Gln Arg Ala Thr Gln Gln Gln Ala Val Ile Glu 180 185 190

Pro Ile Val Thr Thr Asn Trp Gln Lys Leu Glu Ala Phe Trp His Lys 195 200 205

His

- (2) INFORMATION FOR SEQ ID NO: 224:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 12 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (ix) FEATURE:
    - (A) NAME/KEY: Peptide
    - (B) LOCATION: 2..12
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 224:

Ile His Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile
1 5 10

- (2) INFORMATION FOR SEQ ID NO: 225:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 12 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 225:

Val Asn Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 5:
  - (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 12 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 226:

Val Asm Tyr Arg Asm Ala Ser Gly Val Tyr His Ile 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 227:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 12 amino acids
    - (B) TYPE: amine acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEO ID NO: 227:

Val Asn Tyr His Asn Thr Ser Gly Ile Tyr His Leu 1 5 10

- (2) INFORMATION FCR SEQ ID NO: 228:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 12 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 228:

Gln His Tyr Arg Asn Ala Ser Gly Ile Tyr His Val 1  $\,$  5

- (2) INFORMATION FOR SEQ ID NO: 229:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 12 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 229:

Gln His Tyr Arg Asn Val Ser Gly Ile Tyr His Val

- (2) INFORMATION FOR SEQ ID NO: 230:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 12 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 230:

Ile His Tyr Arg Asn Ala Ser Asp Gly Tyr Tyr Ile
1 5 10

- (2) INFORMATION FOR SEQ ID NO: 231:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 12 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 231:

Leu Gln Val Lys Asn Thr Ser Ser Ser Tyr Met Val 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 232:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 11 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 232:

Val Trp Gln Leu Arg Ala Ile Val Leu His Val 1 5 10

(2) INFORMATION FOR SEQ ID NO: 233:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 11 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MCLECULE TYPE: peptide
- (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 233:

Val Tyr Glu Ala Asp Tyr His Ile Leu His Leu 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 234:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 11 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 234:

Val Tyr Glu Thr Asp Asn His Ile Leu His Leu 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 235:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 11 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 235:

Val Tyr Glu Thr Glu Asn His Ile Leu His Leu 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 236:
  - (1) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 11 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 236:

Val Phe Glu Thr Val His His Ile Leu His Leu 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 237:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 11 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (i1) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 237:

Val Phe Glu Thr Glu His His Ile Leu His Leu 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 238:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 11 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 238:

Val Phe Glu Thr Asp His His Ile Met His Leu 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 239:
  - (1) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 11 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 239:

Val Tyr Glu Thr Glu Asn His Ile Leu His Leu 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 240:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 11 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 240:

Val Tyr Glu Ala Asp Ala Leu Ile Leu His Ala 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 241:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 13 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 241:

Val Gln Asp Gly Asn Thr Ser Ala Cys Trp Thr Pro Val 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 242:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 13 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 242:
    Val Lys Thr Gly Asn Gln Ser Arg Cys Trp Val Ala Leu

1 5 10

- (2) INFORMATION FOR SEQ ID NO: 243:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 13 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 243:

Val Lys Thr Gly Asn Gln Ser Arg Cys Trp Val Ala Leu

- (2) INFORMATION FOR SEQ ID NO: 244:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 13 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 244:

Val Arg Thr Gly Asm Glm Ser Arg Cys Trp Val Ala Leu 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 245:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 13 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 245:

Val Lys Thr Gly Asn Gln Ser Arg Cys Trp Ile Ala Leu 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 246:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 13 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 246:
  - Val Lys Thr Gly Asm Glm Ser Arg Cys Trp Ile Ala Leu

1 5 10

- (2) INFORMATION FOR SEQ ID NO: 247:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 13 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (11) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 247:

Val Lys Thr Gly Asn Ser Val Arg Cys Trp Ile Pro Leu 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 248:
  - (1) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 13 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 248:

Val Lys Thr Gly Asn Val Ser Arg Cys Trp Ile Ser Leu 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 249:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 13 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 249:

Val Arg Lys Asp Asn Val Ser Arg Cys Trp Val Gln Ile 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 250:
  - (1) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid

- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 250:

Ala Pro Ser Phe Gly Ala Val Thr Ala Pro
1 5 10

- (2) INFORMATION FCR SEQ ID NO: 251:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (i1) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 251:

Val Ser Gln Pro Gly Ala Leu Thr Lys Gly
1 5 10

- (2) INFORMATION FOR SEQ ID NO: 252:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 252:

Val Lys Tyr Val Gly Ala Thr Thr Ala Ser 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 253:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (11) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 253:

Ala Pro Tyr Ile Gly Ala Pro Val Glu Ser
1 5 10

- (2) INFORMATION FOR SEQ ID NO: 254:
  - (1) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (11) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 254:

Ala Gln His Leu Asm Ala Pro Leu Glu Ser 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 255:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 255:

Ser Pro Tyr Val Gly Ala Pro Leu Glu Pro 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 256:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 256:

Ser Pro Tyr Ala Gly Ala Pro Leu Glu Pro 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 257:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids

- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (X1) SEQUENCE DESCRIPTION: SEQ ID NO: 257:

Ala Pro Tyr Leu Gly Ala Pro Leu Glu Ser 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 258:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 258:

Ala Pro Tyr Leu Gly Ala Pro Leu Glu Ser
1 5 10

- (2) INFORMATION FOR SEQ ID NO: 259:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 259:

Ala Pro Tyr Val Gly Ala Pro Leu Glu Ser
1 5 10

- (2) INFORMATION FOR SEQ ID NO: 260:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 11 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 260:

Asn Val Pro Tyr Leu Gly Ala Pro Leu Thr Ser 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 261:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (i1) MOLECULE TYPE: peptide
  - (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 261:

Ala Pro His Leu Arg Ala Pro Leu Ser Ser 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 262:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 262:

Ala Pro Tyr Leu Gly Ala Pro Leu Thr Ser
1 5 10

- (2) INFORMATION FOR SEQ ID NO: 263:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (i1) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 263:

Arg Pro Arg Gln His Ala Thr Val Gln Asp 1 5 10

(2) INFORMATION FOR SEQ ID NO: 254:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 10 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 264:

Ser Pro Gln His His Lys Phe Val Gln Asp 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 265:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 265:

Arg Pro Arg Arg Leu Trp Thr Thr Gln Glu
1 5 10

- (2) INFORMATION FOR SEQ ID NO: 266:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 10 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 266:

Pro Pro Arg Ile His Glu Thr Thr Gln Asp 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 267:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 14 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 267:

Thr Ile Ser Tyr Ala Asn Gly Ser Gly Pro Ser Asp Asp Lys
1 5 10

- (2) INFORMATION FCR SEQ ID NO: 268:
  - (1) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 19 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - · (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: peptide
  - (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 268:

Ser Arg Arg Gln Pro Ile Pro Arg Ala Arg Arg Thr Glu Gly Arg Ser 1 5 10 15

. Trp Ala Gln

- (2) INFORMATION FOR SEQ ID NO: 269:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 1443 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS,: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: DNA (genomic)
  - (iii) HYPOTHETICAL: NO
  - (iii) ANTI-SENSE: NO
  - (ix) FEATURE:
    - (A) NAME/KEY: CDS
    - (B) LOCATION: 1..1443
  - (ix) FEATURE:
    - (A) NAME/KEY: mat_peptide
    - (B) LOCATION: 1..1443
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 269:

ACC ATC ACC ACC GGA GCT TCT ATC ACA TAC TCC ACT TAC GGC AAG TTC Thr Ile Thr Thr Gly Ala Ser Ile Thr Tyr Ser Thr Tyr Gly Lys Phe

1	5	10	15	
			GAC GTG ATC ATA Asp Val Ile Ile 30	
	s His Ser		CTT GGG ATA GGC Leu Gly Ile Gly 45	
			CTC GTC GTC TTG Leu Val Val Leu 60	
			CAC CCC AAC ATC His Pro Asn Ile	
			TTC TAC GGC AGA Phe Tyr Gly Arg 95	
			CTC ATC TTC TGC Leu Ile Phe Cys 110	
	s Lys Cys		CTG ACC AGC CTG Leu Thr Ser Leu 125	•
			GTC GCC GTC ATC Val Ala Val Ile 140	
			GCG CTC ATG ACG Ala Leu Met Thr	
			AAC TCC GCC GTC Asn Ser Ala Val 175	
			ACC ATT GAG ACT Thr Ile Glu Thr 190	
Thr Val P		Arg Ser Gln	CGT AGG GGC CGC Arg Arg Gly Arg 205	
			TCG GCT GGA GAG Ser Ala Gly Glu 220	
			GAG TGC TAC GAT Glu Cys Tyr Asg G	

										•							
					TAT Tyr 245												768
					AAC Asn												816
					GGG Gly												864
					ACC Thr												912
A					ACA Thr												960
T	'GG				TGG Trp 325	AAA										ACT	1008
					CTC Leu												1056
					CCC				Tyr								1104
					ATT Ile												1152
I					GCC Ala												1200
				Ile	CTC Leu 405	Ser	Gly	Lys	Pro	Ala	Ile		Pro	Asp		Glu	1248
					Gln					Glu					Ser	TTG Leu	1296
				Asp					Ile					Lys		AAA Lys	1344
			Gly					The					a Glu			AAG Lys	1392
		Ala					. Trp					Gl				ACA Thr 480	

TAC 1443
Tyr

- (2) INFORMATION FOR SEQ ID NO: 270:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 481 amino acids
    - (B) TYPE: amino acid
    - (D) TOPOLOGY: linear
  - (11) MOLECULE TYPE: protein
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 270:

Thr Ile Thr Thr Gly Ala Ser Ile Thr Tyr Ser Thr Tyr Gly Lys Phe
1 5 10 15

Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Val Ile Ile Cys
20 25 30

Asp Glu Cys His Ser Gln Asp Ala Thr Thr Ile Leu Gly Ile Gly Thr 35 40 45

Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val Leu Ala 50 60

Thr Ala Thr Pro Pro Gly Ser Val Thr Thr Pro His Pro Asn Ile Glu 65 70 75 80 Glu Val Ala Leu Pro Gln Glu Gly Glu Val Pro Phe Tyr Gly Arg Ala

Ile Pro Leu Ala Phe Ile Lys Gly Gly Arg His Leu Ile Phe Cys His

Ser Lys Lys Cys Asp Glu Leu Ala Lys Gln Leu Thr Ser Leu Gly

Val Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ala Val Ile Pro 130 135 140

Thr Ala Gly Asp Val Val Cys Ser Thr Asp Ala Leu Met Thr Gly 145 150 155 160

Phe Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Ser Ala Val Thr
165 170 175

Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu Thr Thr 180 185 190

Thr Val Pro Gln Asp Ala Val Ser Arg Ser Gln Arg Arg Gly Arg Thr
. 195 200 205

Gly Arg Gly Arg His Gly Ile Tyr Arg Tyr Val Ser Ala Gly Glu Arg 210 215 220

Pro Ser Asp Met Phe Asp Ser Val Val Leu Cys Glu Cys Tyr Asp Ala

								23	<i>د</i>						
225					230					235					240
Gly	Cys	Ala	Trp	Tyr 245	Asp	Leu	Thr	Pro	Ala 250	Glu	Thr	Thr	Val	Arg 255	Leu
			260		Thr			265					270		
Glu	Phe	Trp 275	Glu	Gly	Val	Phe	Thr 280	Gly	Leu	Thr	Asn	Ile 285	Asp	Ala	His
Met	Leu 290	Ser	Gln	Thr	Lys	Gln 295	Gly	Gly	Glu	Asn	Phe 300	Pro	Tyr	Leu	Val
Ala 305	Tyr	Gln	Ala	Thr	Val 310	Cys	Val	Arg	Ala	Lys 315	Ala	Pro	Pro	Pro	Ser 320
Trp	Asp	Thr	Met	Trp 325	Lys	Cys	Met	Leu	Arg 330	Leu	Lys	Pro	Thr	Leu 335	Thr
Gly	Pro	Thr	Pro 340	Leu	Leu	Tyr	Arg	Leu 345	Gly	Pro	Val	Gln	Asn 350	Glu	Ile
Thr	Leu	Thr 355	Hıs	Pro	Ile	Thr	Lys 360	Tyr	Ile	Met	Ala	Cys 363	Met	Ser	Ala
Asp	Leu 370	Glu	Val	Ile	Thr	Ser 375	Thr	Trp	Val	Leu	Val 380	Gly	Gly	Val	Val
Ala 385	Ala	Leu	Ala	Ala	Tyr 390	Cys	Leu	Thr	Val	Gly 395	Ser	Val	Ala	Ile	Val 400
Gly	Arg	Ile	Ile	Leu 405	Ser	Gly	Lys	Pro	Ala 410	Ile	Ile	Pro	Asp	Arg 415	Glu
Ala	Leu	Tyr	Gln 420	Gln	Phe	Asp	Glu	Met 425	Glu	Glu	Cys	Ser	Ala 430	Ser	Leu
Pro	Tyr	Met 435	Asp	Glu	Thr	Arg	Ala 440	Ile	Ala	Gly	Gln	Phe 445	Lys	Glu	Lys
Val	Leu <b>4</b> 50	Gly	Phe	Ile	Ser	Thr 455	Thr	Gly	Gln	Lys	Ala 460	Glu	Thr	Leu	Lys
Pro 465	Ala	Ala	Thr	Ser	Val 470	Trp	Asn	Lys	Ala	Glu 475	Gln	Phe	Trp	Ala	Thr 480
Tyr															

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for scanning.		(Document title)	

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